Functional outcome after excision of heterotopic ossification about the knee in ICU patients

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Abstract The objective of this study was to evaluate the degree of improvement in the range of movement in the knee joint, sitting ability, and overall ambulation in patients with heterotopic ossification of the knee joint who underwent surgical excision of ectopic bone. Between 1999 and 2006, 14 patients (23 joints) with significant heterotopic ossification of the knee joint that required surgery were evaluated. We compared the range of movement in the knee joint, sitting ability, and overall ambulation in the preoperative and postoperative periods using the Fuller and Keenan classification systems. Range of movement increased in 82% of cases (19 knee joints). Sitting ability improved in 13 patients (93%). Postoperatively, ambulation in eight patients (57%) was remarkably superior. In conclusion, resection of heterotopic ossification may significantly improve the range of movement in the knee joint, sitting ability, and overall ambulation.

Résumé Le but de l'étude était d'évaluer l'amélioration de la mobilité, la capacité de s'asseoir et les capacités de déambulation après excision chirurgicale des ossifications hétérotopiques du genou survenues après séjour en réanimation. Quatorze patients (23 genoux) opérés entre 1999 et 2006 sont étudiés en utilisant le système de classification de Fuller et Keenan. L'amplitude de mouvement s'améliore dans 82% des cas (19 articulations). La capacité de s'asseoir s'améliore chez 13 patients (93%) et les capacités de déambulation étaient nettement supérieures chez

8 patients. La résection de ces ossifications hétérotopiques est donc justifiée.

Introduction

Heterotopic ossification is characterised by progressive formation of pathological bone tissue in places where bone is usually not present. It is generally accepted that this mostly affects the periarticular surfaces of large joints [12]. The prevalence of formation of heterotopic bone is 11–75% in adults with brain injury caused by trauma [11].

Development of bone tissue in areas where bone is not normally present has been described after trauma, surgery, or injury to the brain or spinal cord [10]. The overall prevalence of bone formation in patients with brain injury is approximately 20%, but the prevalence of formation of ectopic bone after spinal injury has been described as 16–40% [12]. Heterotopic ossification has been reported in approximately 40% of cases (range, 5–90%) in patients undergoing major hip surgery [2, 6, 7]. Heterotopic ossification is described in approximately 64% of patients with traumatic amputations, with the severe form having a prevalence of 34% [21]. Heterotopic ossification complicates thermal burns in approximately 10% of patients, but significant formation of bone that requires surgery ranges from 0.1 to 3% [13].

The hip joint is believed to be the most commonly affected joint, with a prevalence of 44%; the shoulder and elbow joints have a prevalence of 27% and 26%, respectively. The knee joint is involved in approximately 3% of cases [14]. There are five reports describing surgical excision of ectopic bone tissue from 41 knee joints [4, 8, 9, 12]. We evaluated surgical outcome in 23 knee joints with clinically significant heterotopic ossification.

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Table 1 Patient profiles

Patients	Gender	Age (y)	Associated Injuries	Time spent in ICU (days)	Knee joint affected	Other joints affected
1	M	23	TBI	70	R + L	–
2	M	31	TBI	23	R + L	Hip R
3	M	27	TBI, spleen rupture	31	R + L	–
4	M	44	TBI	37	R + L	Hip R + L Elbow R + L
5	M	42	TBI	55	R + L	–
6	M	29	TBI	18	R + L	–
7	M	36	TBI, T12 fracture	31	R + L	Hip R + L Elbow R
8	M	32	TBI	12	R	Hip R + L Elbow R + L
9	F	26	TBI	36	R	Hip L Elbow L
10	M	19	TBI	150	R	Hip R + L Elbow R + L Ankle R + L
11	M	26	TBI	27	R	Hip R + L Shoulder R
12	M	38	TBI	11	L	–
13	M	32	Acute pancreatitis	41	R + L	Hip R + L
14	M	31	Diphosphonic poisoning	25	R + L	Hip R + L

ICU intensive care unit, TBI brain injury, R right, L left

We sought to evaluate the degree of improvement in the range of movement in the knee joint, sitting ability, and overall ambulation in patients with heterotopic ossification of the knee joint who underwent excision of ectopic bone. We also investigated the influence of heterotopic ossification in other joints on walking.

Materials and methods

From January 1999 to June 2006, 54 consecutive patients (117 joints) with ectopic bone formation that required resection were retrospectively analysed. Of the 117 affected joints, 57 (48.7%) involved the hip, 33 (28.2%) the elbow, 23 (19.7%) the knee joint, three (2.6%) the ankle, and in one case (0.9%) formation of pathological bone tissue involved the shoulder. The adductor muscles of the hip were affected by ossifying myositis in two patients. Patients were admitted to the intensive care unit (ICU) for 5–172 days (mean, 44 days).

Fourteen patients (23 joints) with significant heterotopic ossification in the knee joint that required surgery were studied. Patients were in the ICU for a mean time of 41 days (range, 5–150 days). The age range was 17–52 years (mean, 32 years). There were 13 males and one female (Table 1). Bilateral knee involvement was present in nine patients (Fig. 1). The right knee was predominantly affected in four cases; one patient developed heterotopic ossification in the left joint.

Twelve patients had craniocerebral injury. One patient suffered from acute pancreatitis, and one patient was poisoned by diphosphonic drugs. Only one patient had skeletal trauma; he sustained a compression fracture to the twelfth thoracic vertebra without neurological damage. None of the patients with craniocerebral injury had neurological deficits in the lower extremities.

Nine patients (64%) had associated heterotopic ossification unilaterally or bilaterally in the hip (16 joints); five

Fig. 1 An anteroposterior plain radiograph shows involvement of the anteromedial aspect of both knee joints in a patient admitted to the ICU due to acute pancreatitis

Fig. 2 Anteroposterior (a) and lateral (b) plain radiographs demonstrate a typical pattern of heterotopic ossification located exclusively in the anteromedial aspect of the knee

patients (36%) had heterotopic ossification in one or both elbow joints (eight joints); both ankle joints were affected in one patient (7%); and one patient (7%) had significant heterotopic ossification in his shoulder.

Patients were divided into two groups according to concomitant heterotopic ossification in other joints. Heterotopic ossification was in the knee joint only (one or both knee joints affected) in five patients (group 1). Formation of ectopic bone was present in one or more other joints in nine patients (group 2). Patients who developed heterotopic ossification in more than one joint spent a longer time (mean, 42 days) in the ICU than patients who had heterotopic ossification only in the knee joint (mean, 37 days).

Sitting ability was evaluated using a three-level scale proposed by Fuller et al. [8]. Sitting ability is defined as: (i) “easy” if the patient can sit in a chair or wheelchair without assistance; (ii) “difficult” if the patient can sit in a chair but only with assistance such as cushions, pads, or extensions; and (iii) “unable” if the patient cannot sit in a chair despite assistance.

Overall mobility was recorded using the five-level scale proposed by Keenan et al. [16]. Mobility status is characterised as: (i) “unable” if the patient is physically unable to attempt walking, (ii) “assisted” if another person is needed to assist the patient, (iii) “standby assisted” if the patient can walk but with occasional loss of balance, (iv) “supervised” if the patient requires verbal assistance, and (v) “independent” if the patient can walk safely and independently.

Surgery was done to improve the range of movement in the affected joints. The number of interventions was dependent on the number of the affected joints, the location, and the extent of the lesion (mean, two operations; range, one to six).

With the patient in a supine position, the incision was made in relation to the location of the ossification. A simultaneous anteromedial and lateral approach was made in 11 patients; an anteromedial incision alone was made in three patients (Figs. 2 and 3).

Postoperatively, patients received a prophylactic dose of indomethacin (75 mg, p.o.) for 15 days. Patients who

Fig. 3 a In patients with isolated heterotopic ossification to the anteromedial aspect of the knee, an anteromedial incision was indicated. A large piece of ectopic bone tissue over the medial femoral condyle, contained within the extensor rerinaculum, was excised. b A full range of movement was achieved intra-operatively, immediately after the ectopic bone excision

Table 2 Preoperative and postoperative range of movement (ROM) in the affected knee joints

Patients	Preoperative right knee ROM	Preoperative left knee ROM	Preoperative arch of movement right–left	Postoperative right knee ROM	Postoperative left knee ROM	Postoperative arch of movement right–left
1	40–70	30–70	30–40	10–100	10–120	90–110
2	30–80	40–80	50–40	30–80	20–90	50–70
3	30–50	40–70	20–30	0–110	20–90	110–70
4	40–70	30–50	30–20	20–80	30–50	60–20
5	20–70	30–70	50–40	10–80	10–120	70–110
6	40–70	40–60	30–20	30–100	20–90	70–70
7	30–60	20–70	30–50	30–80	10–100	50–90
8	40–70	Normal range	30	20–90	Normal range	70
9	20–60	Normal range	40	10–100	Normal range	90
10	30–80	Normal range	50	30–80	Normal range	50
11	40–50	Normal range	10	10–110	Normal range	100
12	Normal range	30–60	30	Normal range	10–120	110
13	30–60	30–60	30–30	10–100	10–120	90–110
14	20–70	30–70	50–40	20–70	20–80	50–60

underwent copious knee joint surgery with extensive detachment of soft tissue were treated with postoperative radiation of 7 Gy in a single dose.

The minimum follow-up was 18 months (range, 18–66 months).

Results

Postoperatively, the range of movement increased in 82% of cases (19 knee joints), whereas improvement was not observed in the remaining 18% of cases (four knee joints). Overall, the arc of movement increased from 34.3° to 76.9°. The mean maximum extension of the knee joint improved from 31.7° to 17°; the mean maximum flexion increased from 66.1° to 93.9° (Tables 2 and 3).

Sitting ability was improved by one level in ten patients (71%) and by two levels in three patients (21%). Only one patient had no improvement in sitting ability despite excision. Postoperatively, ambulation in eight patients was remarkably superior, i.e. these patients could walk independently without assistance. Three patients needed the physical assistance of another person; one patient needed another person only because he felt insecure. One patient could walk even though he had recurrent loss of balance. One patient could not walk despite our efforts (Table 4).

Comparing sitting ability in patients with heterotopic ossification located only in the knee joint (group 1) with patients with one or more other joints affected (group 2) we found that the postoperative range of movement was improved in both groups. In group 1, the mean increase of maximum flexion in the knee joint was 20° (from 33.3° to 13.3°); the mean of maximum flexion was increased by 11.4° (from 30.7° to 19.3°) in group 2. The maximum extension improved from 65.5° to 103.3° (37.8° of

improvement) in group 1; the improvement was from 66.4° to 87.8° (21.4° of improvement) in group 2. The arc of movement in group 1 improved from 32.2° to 90° postoperatively, whereas the same increase in group 2 was from 35.7° to 68.5°. Postoperatively, all patients in group 1 improved their sitting ability. Sitting ability in group 1 was improved by two levels in two patients, and by one level in the three remaining patients. Only one patient from group 2 that was initially unable to sit regained this ability after surgery. Most of the patients improved the ability to sit by one level, whereas one patient did not improve his ability postoperatively. Overall ambulation was improved in group 1 by four levels in all patients bar one that gained only two levels in the scale. In group 2, patients improved their mobility including four patients who gained four levels in the scale (one patient gained three levels) and three patients who improved their position by only one level. The patient

Table 3 Postoperative improvement of the range of movement (ROM)

Patient	Right knee ROM	Left knee ROM
1	30–30	20–50
2	None	20–10
3	30–60	20–20
4	20–10	None
5	10–10	20–50
6	10–30	20–30
7	0–20	10–30
8	20–20	Normal range
9	10–40	Normal range
10	None	Normal range
11	30–60	Normal range
12	Normal range	20–60
13	20–40	20–60
14	None	10–10

Table 4 Preoperative and postoperative sitting and ambulatory ability

Patient	Preoperative sitting ability	Postoperative sitting ability	Preoperative ambulatory level	Postoperative ambulatory level
1	Difficult	Easy	Unable	Independent
2	Unable	Difficult	Unable	Assisted
3	Unable	Easy	Unable	Independent
4	Difficult	Easy	Unable	Assisted
5	Difficult	Easy	Unable	Independent
6	Unable	Easy	Unable	Standby assisted
7	Unable	Easy	Unable	Supervised
8	Difficult	Easy	Unable	Independent
9	Difficult	Easy	Unable	Independent
10	Difficult	Difficult	Unable	Unable
11	Difficult	Easy	Unable	Independent
12	Difficult	Easy	Unable	Independent
13	Difficult	Easy	Unable	Independent
14	Difficult	Easy	Unable	Assisted

who did not improve his sitting ability did not improve his ambulation either.

Follow-up at six, 12, and 18 months revealed that, from the 19 joints with improvement in the range of movement, 18 (95%) retained this range. The remaining joint (5%) had a mild deficit in the range that gained promptly postoperatively.

Discussion

Different hypotheses have been proposed to explain the pathogenesis of heterotopic ossification. Major et al. [18] suggested that alterations of the paravertebral venous system may have a significant pathogenetic role in heterotopic ossification in paraplegia based on the similarity in distribution between the course of the venous plexus and the location of the ossific deposits in neurological diseases. It is generally believed that the pathogenesis of heterotopic ossification involves three requisite components: (i) inductive signalling pathways, (ii) inducible osteoprogenitor cells, and (iii) a heterotopic environment conducive to osteogenesis [14]. Recently, Kaplan et al. [15] proposed that cells of haematopoietic origin may contribute to the formation of an ectopic skeleton, although they cannot initiate the process alone. According to their theory, at least two populations of connective tissue cells, one derived from circulating cells of haematopoietic origin and another derived from an osteogenic connective tissue–progenitor population, are necessary to form an ectopic skeleton.

Many risk factors have been proposed which may participate in the pathogenesis of bone formation. The

potential risk factor of being male is controversial. With trauma occurring predominately in males, many authors noticed statistical significance in the occurrence of heterotopic ossification in male patients, although there was no difference between the sexes in other studies [1, 21]. In our study, the percentage of affected men was remarkably higher. Our study indicates a potential affiliation between young age and heterotopic ossification, but age does not appear to affect the occurrence of the formation of ectopic bone in most studies.

The exact mechanism of ectopic ossification in patients treated in the ICU is unknown. Heterotopic ossification in these patients has been rarely reported [17]. In our series, most patients were admitted to the ICU due to trauma to the brain, but two patients did not have neurological injury.

Plain radiographs followed by CT are the most valuable diagnostic tools for heterotopic ossification. Ultrasonography has been previously used for early diagnosis. MRI is considered to be the first-line method for soft tissue lesions. MRI is an important diagnostic tool in the early diagnosis of heterotopic ossification because it can detect early signs of heterotopic ossification shortly after the onset of clinical symptoms and if conventional radiographs are negative [3].

The hip joint is usually affected. According to Garland et al. [12], the knee joint is involved in approximately 3% of cases. We found a prevalence of 20% for clinically important heterotopic ossification around the knee joint. This is significantly higher than that reported in the literature.

This study analysed the relationship of heterotopic ossification in multiple joints with sitting and ambulation. We found a significantly higher improvement in the

Fig. 4 Even when immature ectopic bone is still present, indicated by increased uptake during bone scintigraphy, surgical excision is indicated if the patient's neurological status is stabilised

increase of maximum knee flexion and extension in patients who had isolated knee joint ossification than that seen in patients with multiple heterotopic ossification.

Overall, sitting ability as well as ambulation of patients in group 1 was better than that of patients in group 2, both preoperatively and postoperatively. Improvement of mobility after surgery was also higher in the group of patients with isolated knee joint ossification. Factors such as the ability to use upper extremity aids, pain, and stiffness in other joints also reduce independent mobility.

The optimal time for surgery is controversial. Until recently, surgery was delayed for 12 months after increased uptake on a bone scan had stopped to allow maturation of ectopic bone and thus minimise the risk of recurrence of the lesion. Melamed et al. [19] stated that recurrence of heterotopic ossification after excision is unlikely, even if increased uptake during bone scintigraphy is present (Fig. 4). Delayed surgery is contraindicated because of the increased risk of fracture due to local osteoporosis [22]. Stabilisation of neurological status should also be considered with regard to the timing of surgery. Garland et al. [12] proposed a longer time for resection of ectopic bone in head-injured adults because patients with brain injury continue to improve neurologically for a longer period than patients with spinal cord trauma.

Recurrence of heterotopic ossification postoperatively in patients who did not receive prophylaxis raises the question of the effectiveness of radiation, indomethacin, or nonsteroidal antiinflammatories (NSAIDs) in heterotopic ossification after brain injury or in patients admitted to the ICU [9]. Indomethacin, as a prostaglandin inhibitor, has been widely used for the prevention of formation of ectopic bone. Radiation has been proven to significantly decrease heterotopic ossification after total hip replacement if used postoperatively. Different radiotherapy regimens have been suggested since Coventry and Scanlon [5] proposed that postoperative radiation reduces the occurrence of ectopic bone formation. Preoperative radiotherapy has the advantages of easy transportation and of patient positioning compared with the immediate postoperative period, and it does not carry the potential risk of severe postoperative complications [24]. Neurological injury has been associated aetiologically with heterotopic ossification, so postoperative irradiation was administered in a single dose in these patients.

Our experience of NSAIDs is in agreement with the studies in which NSAIDs have been used with encouraging results in the postoperative period to prevent the formation of heterotopic ossification around the knee joint [4]. In general, with the exception of aspirin, most NSAIDs used in medium-to-high dosage regimens showed an approximate relative reduction in postoperative heterotopic ossification of 57% [20]. Recently, selective cyclooxygenase-2 (COX-2) inhibitors were shown to be more effective in the

prevention of formation of ectopic bone than ibuprofen [23]. These results, in addition to the reduced gastrointestinal side effects, suggest that, after excision of ectopic bone formation, a short period of prophylaxis with COX-2 inhibitors may be the preferred treatment for prevention of recurrence of heterotopic ossification.

Conclusion

Surgical excision of the ectopic bone around the affected knee significantly improves the range of movement of the joint, sitting ability, and overall ambulation of patients with heterotopic ossification. Comparing surgical outcome in patients with ectopic bone located solely in the knee joint with patients with heterotopic ossification in multiple joints, we identified impairment of postoperative improvement in patients with affected adjacent joints. Surgical excision provides a superior quality of life in these patients because they have a high risk of major complications due to their poor level of mobility.

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