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Original article

Long-term results of bipolar hemiarthroplasty for osteoarthritis of the hip and idiopathic osteonecrosis of the femoral head

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Abstract

Background. Satisfactory results have been reported from long-term studies on bipolar hemiarthroplasty for femoral neck fracture. However, long-term results of this procedure for osteoarthritis of the hip (OA) and idiopathic necrosis of the femoral head (ION) have given rise to pessimism. These poor results have often reported migration of the bipolar head, but few had described the direction of this migration. The purpose of the present study was to conduct a long-term follow-up analysis of bipolar hemiarthroplasty for OA and ION, including the direction of migration.

Methods. We retrospectively reviewed a consecutive series of 64 patients (76 hips) who underwent primary bipolar hemiarthroplasty for symptomatic OA and ION with a cementless femoral component between 1976 and 1995. Of these 64 patients, 35 patients (40 hips) were available for clinical and radiographic review at a minimum follow-up duration of 10 years.

Results. The Japanese Orthopaedic Association score significantly improved and pain relief was high following surgery; however, preservation of acetabular bone stock could not be achieved because of migration. The survival rate declined 10 years after surgery. Superomedial migration was found to be a risk factor for revision, and one factor affecting superomedial migration was the postoperative center edge angle.

Conclusions. The long-term results of bipolar hemiarthroplasty for OA and ION are not favorable. If a sufficient centripetal position is obtained with reaming, the bipolar head tends to migrate superomedially, subsequently requiring revision.

Introduction

Bipolar hemiarthroplasty was initially advocated for the treatment of acute fractures of the femoral neck and/or nonunion of femoral neck fractures, and good outcomes have been reported: The 10-year survival rate after bipolar hemiarthroplasty for femoral neck fracture is approximately 90%.[1,2] The advantages of bipolar hemiarthroplasty compared to total hip arthroplasty are that the surgical procedure is simple, the volume of blood loss is small, and the incidence of dislocation is low.

Several authors have reported good to excellent short-term and intermediate-term results in association with the use of bipolar hemiarthroplasty for osteoarthritis of the hip (OA) and idiopathic osteonecrosis of the femoral head (ION).[3–5] However, many reports on mid- to long-term results demonstrated unacceptably high rates of pain, migration, osteolysis, and the need for revision to total hip arthroplasty.[6–12] There have been no reports evaluating the direction of migration, either superomedially or superolaterally. The objective of this study was to analyze the long-term outcomes of bipolar hemiarthroplasty applied to OA and ION, including the direction of migration.

Materials and methods

Patients

We retrospectively reviewed a consecutive series of 64 patients (76 hips) who underwent primary bipolar hemiarthroplasty for the treatment of symptomatic OA and ION with a cementless femoral component between 1976 and 1995. Among them, 11 patients (12 hips) were lost to follow-up before 10 years, 10 patients (14 hips) died, 3 patients (4 hips) were not able to be directly examined, and 5 patients (6 hips) were those for whom data at the initial surgery was incomplete. This left 35 patients (40 hips) who had a minimum follow-up duration of 10 years to serve as study subjects. There were 10 hips in 10 male patients and 30 hips in 25 female patients: 16 hips in 15 patients with OA and 24 hips in 20 patients with ION (16 hips at stage III, 8 hips at stage

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IV). The mean follow-up period was 13.7 years (range 5.9–24.9 years), including patients with a follow-up of less than 10 years due to revision within 10 years after the initial surgery). The mean patient age at the time of surgery was 48.8 years (range 25–77 years).

Surgery was performed through the posterolateral approach. Acetabular reaming was performed in the 23 hips (OA, 15; ION stage III, 6; ION stage IV, 2). Bone grafting of the acetabulum from the femoral head was performed with acetabular reaming in 12 dysplastic hips. All bone grafts were blocks and were fixed using two or three AO cortical screws. Regarding the models used, HS11 (Osteonics, Allendale, NJ, USA) was used in 22 hips; Bateman UPF 1 (3M, St. Paul, MN, USA) was used in 10 hips; and Anatomic (Zimmer, Warsaw, IN, USA) was used in 8 hips.

Methods

We evaluated the Japan Orthopaedic Association (JOA) scores before surgery and at the time of the final follow-up. For revision cases, we used the values before revision. We also evaluated the survival rates, using the Kaplan-Meier method with revision as the endpoint, and the causes for revision. For risk factors for revision, the following items were examined: sex, body weight, age at the time of surgery, preoperative and postoperative JOA scores, underlying diagnoses, the device used, reaming conducted or not conducted during surgery, and the use of a bone graft. Furthermore, for factors that may affect the direction of migration, the following items were evaluated: postoperative center edge (CE) angle including the grafted bone; postoperative leg-length discrepancy; postoperative distance between the iliopectineal line and the center of the bipolar head; reaming conducted or not conducted during surgery; use of a bone graft. The distance of migration and the revision rate were also evaluated.

The radiographs were evaluated with regard to the distance of migration of the bipolar head and its direction. To measure the distance of migration, we drew a line connecting the teardrops on both sides of a plain radiograph (anteroposterior view), dropped a perpendicular line from the center of the bipolar head, measured the vertical and horizontal distances from the teardrops, and calculated the square root of the difference between the value immediately after the initial surgery and the value at the time of the final follow-up or immediately before revision (Fig. 1). The migration to an upper medial direction of the bipolar head was called superomedial migration and that to the upper lateral direction superolateral migration. The study protocol was approved by the committee on ethics and the institutional review board of Mie University Graduate School of Medicine.

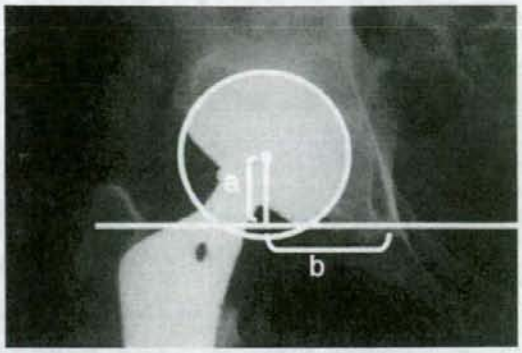

Fig. 1. Measurement of the distance of migration: Measurement of distance of migration = $\sqrt{(a2-a1)^2+(b2-b1)^2}$

Statistical analysis

Data were analyzed with the Statview software program, and the level of significance was set at $P = 0.05$ for all analyses. Differences in factors were analyzed by the t statistic for continuous variables and by the χ^2 statistic for dichotomous variables. Kaplan-Meier analysis was used to establish the survival of the individual arthroplasty components. Censored data in the Kaplan-Meier analysis included those for patients (hips) who had died, those who had been lost to follow-up, and those who had been followed for less than 10 years without having undergone revision of the index replacement.

Results

The mean JOA score before surgery was 48.4 ± 13.0 and that at the time of the final follow-up was 78.3 ± 11.1, which indicates significant improvement ($P < 0.0001$). Only two patients had severe pain at the time of revision. The mean JOA scores at the time of the final follow-up of the patients who did not undergo revision was 78.9 ± 11.7, and the mean score immediately before revision of the patients who underwent revision was 77.8 ± 10.5; no significant difference was observed.

Nineteen patients (21 hips) required revision within the follow-up period. The mean period before revision was 11.7 years (range 5.9–20.1 years). Regarding survival rates with revision as the endpoint, the survival rate was 81% at 10 years, 56% at 15 years, and 32% at 20 years (Fig. 2). Regarding the causes for revision, migration on the acetabular side accounted for 17 of 21 hips. Revisions due to problems on the stem side were performed in the other 4 hips. The relations between the surgical procedure and the distance of migration, revision rate, and direction of migration are compiled

Table 1. Relations between the surgical procedure and the distance of migration, revision rate, and direction of migration

Reaming status	No. of hips	Distance of migration (mm)	Revision rate (%)	Direction of migration (no. of hips)	
				Superomedial	Superolateral
No reaming	17	1.86 ± 1.45 (0.20–6.27)	41.2	8	9
Reaming	23	5.27 ± 3.28 (1.43–13.16)	60.9	13	10

Data given as mean ± SD (minimum–maximum)

Table 2. Relation between the direction of migration and the distance of migration, revision rate, and central edge angle

Direction of migration	No. of hips	Distance of migration (mm)	Revision rate		CE angle (°)	
Superomedial	21	4.02 ± 3.23 (0.60–13.16)	71%	$P = 0.0117$	47.619 ± 18.413	$P = 0.0439$
Superolateral	19	3.59 ± 3.04 (0.20–10.99)	32%		37.895 ± 10.044	

Data given as mean ± SD (minimum–maximum)
CE, central edge

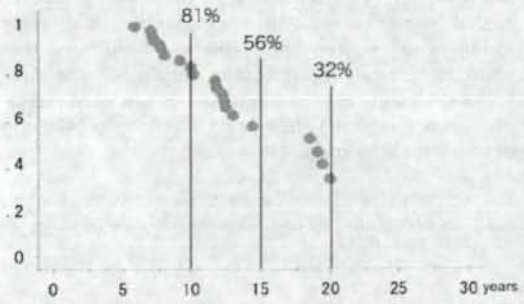

Fig. 2. Survival rates with revision as the endpoint were 81% at 10 years, 56% at 15 years, and 32% at 20 years

in Table 1. The mean distance of migration in those who underwent reaming was greater than in those who did not ($P < 0.0001$).

Significant risk factors for revision were the direction of migration and the stage of ION. The revision rate was 71% for superomedial migration and 32% for superolateral migration, indicating a significantly higher percentage for superomedial migration ($P = 0.0117$). In cases of superolateral migration, revision was often performed owing to interference with screws used for the bone graft; and in cases of superomedial migration, revision was often performed considering the risk of perforation while getting closer to the iliopectineal line (Fig. 3). A significant risk factor affecting the superomedial migration was the postoperative CE angle ($P = 0.0439$) (Table 2).

The revision rate was 44% in patients with ION stage III and 88% in patients with ION stage IV, indicating a significantly higher percentage of revisions among patients with stage IV ION ($P = 0.0404$) (Table 3).

Table 3. Revision rate of hips with idiopathic osteonecrosis by stage

ION stage	No. of hips	Revision rate	
III	16	44%	$P = 0.0404$
IV	8	88%	

ION, idiopathic osteonecrosis

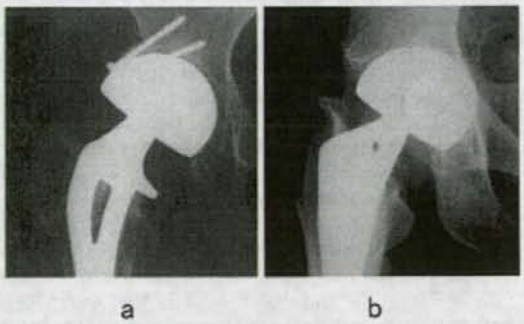

Fig. 3. Direction of migration. **a** With superolateral migration, revision was often performed owing to interference with the screws used for the bone graft. **b** With superomedial migration, revision was often performed taking into considering the risk of perforation when getting close to the iliopectineal line

Discussion

Several authors have reported good to excellent short-term and intermediate-term results in association with the use of the bipolar arthroplasty for the treatment of degenerative and inflammatory conditions of the hip.[3,4] A shorter operating time and ease of revision were cited

as particular benefits of the prosthetic design. Yamamuro et al.,[13] in a report on 35 patients with a mean age of 41 years, concluded that results are not compromised by younger age. Cabanela[14] and Hanssen et al.[15] examined the use of bipolar arthroplasty and total hip replacement in patients with ION and concluded that although a fixed porous-coated acetabular component was associated with better symptomatic relief and a lower failure rate in comparison with bipolar hip arthroplasty at a mean follow-up of 9.2 years, the results of both types of arthroplasty were generally satisfactory. In addition, Kindsfater et al.[16] reported a prosthetic survival rate of 95% at 8 years in a general group of patients with osteoarthritis. Collectively, these series suggest that the intermediate-term clinical results of bipolar hip arthroplasty are satisfactory, independent of age, and that the underlying diagnosis generally does not have an influence on the outcome. In contrast to these generally positive reports, our longer-term review at a minimum of 10 years postoperatively demonstrated a higher prevalence of acetabular failure than has been seen in association with contemporary total hip arthroplasty after comparable periods of follow-up. The JOA score significantly improved, and pain relief was high ($P < 0.0001$), but there was also a high incidence of bone defects associated with migration, necessitating revision. Consequently, the expected preservation of acetabular bone stock was not achieved.

Pellegrini et al. reported that when the acetabulum was reamed at the time of the index arthroplasty there was a greater risk of revision.[6] The satisfactory results reported by Nagai et al.[17] at a long-term follow-up was limited to patients who did not undergo reaming of the acetabulum. Among our patients, the mean distance of migration in those who underwent reaming was greater than for those who did not; and the direction of migration was one of the significant risk factors for revision. The pain was not severe in association in either direction of migration, and the JOA score was not exacerbated. In cases of superomedial migration, however, when migration progressed, acetabular bone stock was severely decreased, and some patients were at risk of perforation of the inner table. Therefore, the decision for revision was not prolonged. In contrast, with superolateral migration, the acetabular bone stock was comparatively maintained even if migration had progressed. The decision of revision was prolonged in many cases until we had misgivings about metallosis due to interference with the screws. Such decisions may be why the revision rate was significantly different regarding the direction of migration.

Despite an extensive search, we could not find studies that divided the direction of migration into the superomedial and superolateral directions. When hemiarthroplasty is performed for ION, it has been reported that migration hardly progresses in the hips with up to stage III ION without osteoarthritic change;[18,19] however, it is also reported that degenerative changes are already present in the acetabular cartilage of all hips with ION stage III histologically, even when plain radiographs of the acetabulum show no abnormalities.[20] In this study, the revision rate was 44% with stage III ION and 88% with stage IV.

Conclusion

At 10 years after bipolar hemiarthroplasty the survival rate declined, and we found poor long-term results with bipolar hemiarthroplasty for OA and ION. There was no significant relation between the distance of migration and the direction of migration; but when migration developed superomedially, the revision rate was significantly higher. A significant factor determining superomedial migration was the postoperative CE angle including the grafted bone. This study indicated that when the surgical procedure is accompanied by reaming and a sufficient centripetal position is obtained migration occurs superomedially, resulting in a subsequent need for revision surgery.

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Asymptomatic disseminated carcinomatosis of bone marrow presenting as hyperphosphatasia : report of a case

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Abstract

Metastatic involvement of the musculoskeletal system is one of the most significant clinical issues facing orthopaedic oncologists. The number of patients with metastasis to the skeletal system from a carcinoma is 15 times greater than the number of patients with primary bone tumours of all types. However, progression patterns like disseminated carcinomatosis of bone marrow are comparatively rare. The pathophysiology for disseminated carcinomatosis of bone marrow, with a prognosis reported to be very poor, is still unknown. We describe a patient who had no symptoms with hyperphosphatasia. Bone scintigraphy showed a so-called super bone scan and a needle biopsy from the ileum showed adenocarcinoma cells. Additional endoscopic investigation was performed and signet cell gastric cancer was found. From the bone scan and biopsy, we established the diagnosis of disseminated carcinomatosis of the bone marrow. From the experience of this case, we believe that intensive stomach investigation should be considered in cases with hyperphosphatasia, even when the patient has no symptoms. (Acta gastroenterol. belg., **2008**, 71, **271-274**).

Key words : disseminated carcinomatosis of bone marrow, hyperphosphatasia, gastric cancer.

Introduction

Metastatic involvement of the musculoskeletal system is one of the most significant clinical issues facing orthopaedic oncologists. The number of patients with metastasis to the skeletal system from a carcinoma is 15 times greater than the number of patients with primary bone tumours of all types. However, progression patterns like disseminated carcinomatosis of bone marrow are comparatively rare (1). The pathophysiology for disseminated carcinomatosis of bone marrow, with a prognosis reported to be very poor, is still unknown. We report a rare case of asymptomatic disseminated carcinomatosis of bone marrow presenting as hyperphosphatasia.

Case report

A 65-year-old woman was admitted to our hospital for a second opinion, due to a 2-year history of hyperphosphatasia. She had no back pain or any other symptoms.

In 2004, she was found to have a serum ALP level of 800 IU/l by a family practitioner. At that time, from physical examination and laboratory findings, obstructive hepatobiliary diseases, hyperparathyroidism, and hepatotoxic drugs were ruled out. However, osteosclerotic lesions in the thoracic vertebrae and lumbar vertebrae were recognised, so bone diseases were suspected. The patient was referred to a state hospital, where healthcare personnel carried out tumour marker studies (CEA, CA19-9), magnetic resonance imaging (MRI), bone scan, and positron emission tomography (PET). The test results showed increased uptake in the spine and ribs in the bone scan, but tumour markers were negative and there were no abnormal findings with MRI or PET. The logical conclusion at that time was Paget's disease, and the condition was treated with bisphosphonates. The ALP level decreased slightly, but later it increased again. Consequently, the patient was referred to our institution.

She had a past medical history of fatty liver disease, hypertension, gastritis, benign ovarian tumour, and cataract but no history of cancer. At the physical examination, the patient appeared to be a well developed female in no apparent distress (temperature 36.5°C, pulse 69 beats/min, blood pressure 160/63 mmHg), with no deformities in her thoracic to lumbar spine, nor was there local heat or tenderness. The range of motion in her limbs was not restricted. Neurologically, muscle power in both upper and lower extremities was well preserved and there were no sensory disturbances. Reflexes were also normal.

The results of hematological examination and other laboratory tests are shown in Table 1. Although the serum calcium and phosphorus levels were within normal ranges, the ALP level was extremely high, 6267 IU/L. Isoenzyme separation showed a markedly increased amount of bone isoenzyme. Levels of tumour markers CEA and CA19-9 were normal.

Plain radiographs showed multiple osteosclerotic lesions in the spine and pelvis that were not detected eight months earlier (Fig. 1). Magnetic resonance imaging showed low signal intensities on the T1- and T2-weighed images in the lumbar spine, but there was no obvious abnormality. The Tc-99m MDP bone scan showed increased uptake in the whole spine, pelvis, and

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Table 1. — **Laboratory findings**

	Patient's results	Reference interval
White cell count (/μl)	7350	4000-9000
Red cell count (× 10^4/μl)	327	380-480
Haemoglobin (g/dl)	9.1	12.0-17.5
Haematocrit (%)	29.6	35-45
Platelets (× 10^4/μl)	14.8	15-45
Activated partial thromboplastin time (s)	24.7	25-35
Prothrombin time (s)	12.6	11-15
Total protein (g/dl)	7.1	6.0-8.0
Albumin (g/dl)	4.3	3.4-4.7
Asparate aminotransferase (IU/L)	21	0-35
Alanine aminotransferase (IU/L)	16	0-35
Lactate dehydrogenase (IU/L)	290	88-230
Cholinesterase (pH)	0.99	0.8-1.1
γ-gultamyl transpeptidase (IU/L)	232	9-85
Alkaline phosphatase (IU/L)	6267	41-133
Total bilirubin (mg/dl)	0.5	0.1-1.2
Total cholesterol (mg/dl)	228	< 200
Blood urea nitrogen (mg/dl)	13	8-20
Creatinine (mg/dl)	0.7	0.6-1.2
Sodium (mEq/l)	141	135-145
Potassium (mEq/l)	4.3	3.5-5.0
Calcium (mg/dl)	10	8.5-10.5
Phosphate (mg/dl)	3.9	2.5-4.5
Glucose (mg/dl)	103	60-110
Creatine kinase (IU/L)	57	12-170
C-reactive protein (mg/dl)	0.32	0-2
Carcinoembryonic antigen (ng/dl)	4.8	0-5.0
Carbonhydrate antigen 19-9 (U/ml)	1	< 37

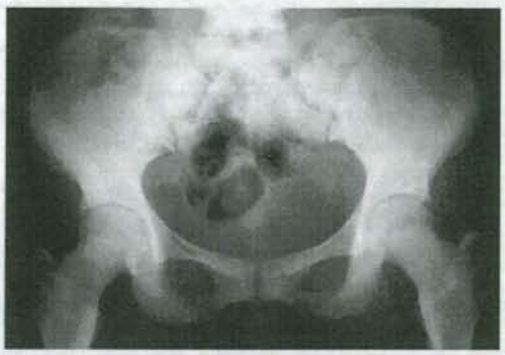

Fig. 1. — Radiograph of the pelvis shows multiple osteosclerotic lesions.

ribs (Fig. 2). On the other hand, no increased uptake was seen in the kidney, which could be interpreted as the so-called super bone scan. Positron emission tomography showed no abnormality. To make a histological diagnosis of the sclerotic bone lesions, needle biopsy was carried out from the ileum (Fig. 3). Microscopically, there were small atypical cells with signet ring cell features. The pathological diagnosis was metastasis of 'signet ring' adenocarcinoma.

Endoscopy was performed and multiple gastric mucosal lesions were found. Biopsy of the lesions showed a poorly differentiated 'signet ring' adenocarcinoma. The tumour was in the form of individual signet ring cells with large mucin vacuoles, resembling the cells seen in the needle biopsy carried out from the ileum.

The patient was moved to the chemotherapy unit and treatment with MTX-5FU commenced. Twenty courses of MTX 100 mg/m² and 5-FU 130 mg/m² were given and the patient's ALP level decreased to 1708 IU/L. Recently, her ALP level has increased again and weekly paclitaxel (PTX) was started ; the patient has been treated by outpatient care for more than one year.

Discussion

This patient had no past history related to cancer and her tumour markers were negative. Furthermore, she did not report any symptom related to the gastrointestinal system or any pain related to the bone metastases. In many cancer patients, pain is the first symptom, and 75-90% of patients with metastatic or advanced cancer will experience significant amounts of pain (2). In addition, 35-42% of cancer patients have cancer-related bone pain (3,4). The possible mechanisms of bone pain are the release of chemical mediators such as prostaglandin, the increased pressure within the bone, microfractures, and nerve invasion. Typical radiographic features show lytic, sclerotic, or mixed metastases that are responsible for osteoclast activation (5). In bone metastases, osteoclasts secrete acid and cause bone resorption from tumour invasion. In this case showing sclerotic metastases, there may have been little activity of the nociceptor, which senses acid stimulation induced by osteoclasts and mechanical stimulation by bone resorption (2,6).

Fig. 2. — Bone scintigraphy shows a so-called super bone scan. Note the markedly increased uptake of the radionuclide in the whole spine and the absence of renal sign.

In this case, the only abnormal finding was hyperphosphatasia. This was the key to diagnosis. Alkaline phosphatase increases in obstructive hepatobiliary disease, bone disease (physiologic bone growth, Paget's disease, osteomalacia, osteogenic sarcoma, bone metastases), hyperparathyroidism, rickets, benign familial hyperphosphatasemia, pregnancy (third trimester), GI disease (perforated ulcer or bowel infarct), and cases of hepatotoxic drugs. Only a few reports have been published concerning multiple metastases of unknown origin with hyperphosphatasia (7-10). Tokushima *et al.* suggested that the cancer cells themselves might produce ALP (10). However, the pathogenesis and pathological

Fig. 3. — Histological examination of the iliac biopsy shows a number of small atypical cells with signet ring cell features (H&E, × 100).

roles of ALP in such cases are still unknown. For the differential diagnosis, a whole body bone scan was performed, which showed abnormal findings, a so-called 'super bone scan'. A super bone scan is defined as intense symmetric activity in the bones and diminished renal parenchymal activity (11). Sy *et al.* hypothesized that the increased uptake of radiopharmaceutical by diseased bone results in reduced phosphate excretion, thereby producing faint renal images in the bone scan (12). Such appearances have been reported to be common in delayed imaging (in normal patients), metastases (most frequently in prostate and breast cancers), and renal osteodystrophy (7). Thrupkaew *et al.* reported that cases of diffuse metastatic disease showed a super bone scan (13). Though rare, there are a few reports about super bone scan due to metastatic gastric cancer (14,15).

In 1936, Jarcho first described a special group of patients with diffusely infiltrating carcinoma of the stomach, showing a number of common features (16). Forty Japanese patients were reviewed by Hayashi *et al.* in 1979 for what was called "disseminated carcinomatosis of the bone marrow" (17). The primary tumour was gastric cancer in 37 of these 40 patients (92.5%). Pathological diagnosis was obtained in 33 patients, 27 of whom showed either poorly differentiated or mucin-producing adenocarcinoma. There were two peaks in age distribution, in the thirties and fifties, and one-fourth of the patients were women under 40 years of age. The triad of symptoms was related to anemia (85%), bleeding tendency (65%), and low back pain (67.5%). Hematological examination often showed severe anemia and leukocytosis with leukoerythoblastosis. Up to 90% of cases were accompanied by microangiopathic hemolytic anemia or disseminated intravascular coagulation. Blood chemical tests revealed marked elevation of ALP and lactate dehydrogenase in most cases.

From the bone scan and biopsy, we established the diagnosis of disseminated carcinomatosis of the bone marrow. The prognosis of this condition has been reported to be very poor (7-10,18). The mean survival after diagnosis is 2.3 months. There are few reports that chemotherapy provides relief in patients with bone carcinomatosis from gastric cancer. Sequential MTX-5FU treatment seems to be one of the most effective regimens for gastric cancer. Chemotherapy with 600 mg/m^2 of 5-FU and 100 mg/m^2 of MTX was more effective for patients with poorly differentiated carcinoma compared with differentiated adenocarcinoma, showing a response rate of 50% (19). Efficacy of chemotherapy can also be expected in cases complicated by disseminated intravascular coagulation, but even so, the patient' survival time is no more than 5-19 months (8).

In this case, we were able to find the cause of the disease and begin chemotherapy. Different chemotherapy regimens were carried out at the primary site. From the experience, we believe that bone scans and intensive stomach investigations should be considered in cases with hyperphosphatasia and multiple osteosclerotic lesions, even when a patient has no symptoms. There is a possibility of disseminated carcinomatosis of bone marrow and if there is a super bone scan, biopsy should be carried out because accurate treatment will prolong the prognosis. The reason why this tumour grows slowly is still unknown and further study is needed.

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Short communication

Total knee arthroplasty in osteogenesis imperfecta: Case report

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Abstract

Osteogenesis imperfecta (OI) is a rare congenital disorder of type I collagen production that results in brittle bones and affects body systems containing collagen. The increasing life span of patients with OI has recently revealed a high incidence of osteoarthritis of the knee. A 53 year-old man with OI presented with bilateral knee pain. He had severe deformities of the proximal part of the femur with subsegment post-traumatic osteoarthritis of both sides of the knees. However, the frequency of fracture gradually decreased and he had not experienced a fracture for 17 years. His bone mineral density was extremely low for his age. He underwent cemented total knee arthroplasty (TKA) on the left knee. One year later, the patient had relief of pain and he could walk without assistance. To our knowledge, only three knee replacements in two patients with OI have been reported, so this case is extremely rare. Although whether a patient with OI is a suitable candidate for knee replacement, it was a useful treatment for osteoarthritis in this case.

Keywords: Osteogenesis imperfecta; Total knee arthroplasty; Joint osteoarthritis; Dwarfism; Osteoporosis

1. Introduction

Osteogenesis imperfecta (OI) is an inherited disorder of type I collagen that presents as short stature, blue sclerae, and hearing defects [1]. The major orthopedic complications include osteoporosis, fracture, non-union of fractures, protrusio acetabuli, spinal involvement, shortened of trunk, ligament laxity and deformity or malalignment of limbs [2]. The increased life span of patients with OI who can walk has recently revealed that they develop osteoarthritis in adulthood. To our knowledge, only three knees have been replaced in patients with OI [3]. Extra-articular deformities of others have been relatively mild but this case was severe.

We describe one-stage total knee arthroplasty (TKA) in a patient with severe extra-articular deformity and knee osteoarthritis with osteogenesis imperfecta.

2. Case report

A 53 year-old man with OI presented with 10-year history of pain in the left knee. He was diagnosed with type III OI during early childhood because of short stature, blue sclerae and multiple fractures [4]. However, the frequency of fractures gradually decreased throughout adolescence and he had none over the previous 17 years. At the time of presentation he was 119.7 cm tall and weighed 39.2 kg. Bone mineral density (BMD) of the lumbar vertebrae (L2-4) evaluated by dual-energy X-ray absorptiometry (DEXA) was 0.577 g/cm^2 and the T-score was 55%. Bone fragility had never been addressed with medication. His left knee had a valgus deformity with a range of motion from 15° to 120°. X-rays revealed osteoarthritis of the bilateral knee from repeated malaligned fractures (Fig. 1). The femorotibial angle of the remarkably small knee was 156°. The knee score and functional score (Knee Society scoring system) were 20 and 40 points, respectively [5]. Conservative management including anti-inflammatory drugs, a knee brace, physical therapy and intra-articular hyaluronic acid injection did not relieve symptoms to much extent.

During March 2005, he underwent left cemented TKA with the PFC Sigma total knee system (Depuy Orthopaedics, Warsaw, Ind.) without computer navigation. This procedure was accomplished using total knee components that retain the cruciate ligaments because the posterior cruciate ligament was intact and posterior-stabilized total knee components were too large for our patient. The intramedullary guide rod could be

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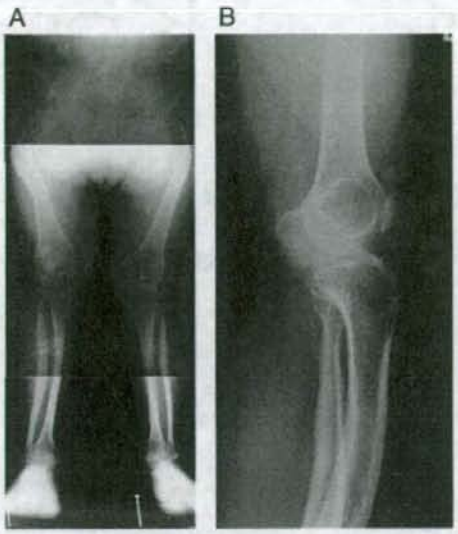

Fig. 1. Preoperative radiographs. Both legs in standing position (A) and lateral view (B).

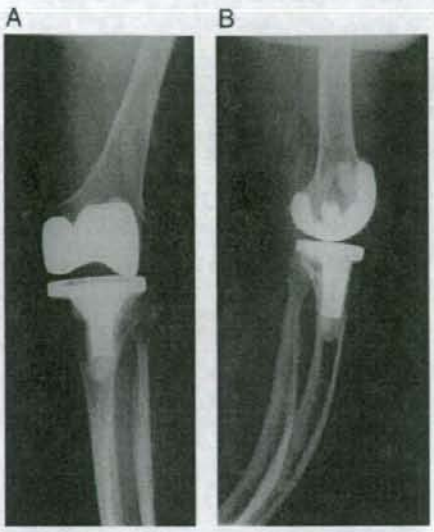

Fig. 3. Radiographs at 1 year after surgery. Anteroposterior (A) and lateral (B) views.

applied on the femoral, but not the tibial side due to tibial deformity arising from repeated fractures. The tibia was cut using an extramedullary guide. Because the mechanical axis ran near the center of the knee, the distal femoral bone was cut with the same alignment. The rotational alignment of the corresponding cutting block is determined using the transepicondylar axis. The tibia cut was perpendicular to the tibial axis. The patella was not resurfaced because degenerative change was negligible. The polyethylene insert used to retain the cruciate ligaments was 8 mm. Neither medial nor lateral release was performed. The motion after joint closure ranged from full extension to 100° of flexion. Histological findings of the articular surface showed thin subchondral bone and a few, abnormally thin trabeculae (Fig. 2). The patient recovered uneventfully. Continuous passive motion was not applied due to the shortness of the patient's leg. To treat his osteoporosis, oral alendronate (2.5 mg/day) and alfacalcidol (1 μg/day) were prescribed.

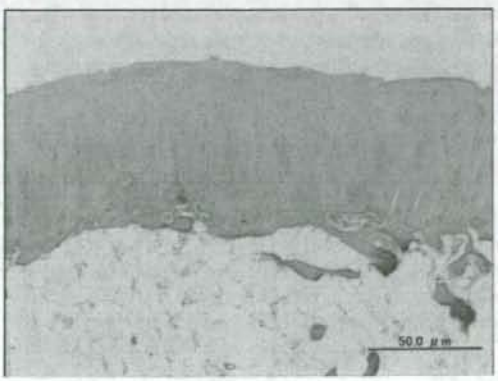

Fig. 2. Histological findings of knee surface.

One year later, the knee was pain-free and the patient could walk unaided. The active range of motion from 0°–90° was painless and collateral stability was normal. Radiography revealed satisfactory alignment without signs of implant loosening (Fig. 3). The knee score and function score improved to 71 and 80 points, respectively.

3. Discussion

The life span of patients with osteogenesis imperfecta has increased, and osteoarthritis of the knee has become common in adult patients with OI who can walk despite osseous deformities. The joints of the extremities in these patients are affected by two processes that can lead to premature degenerative joint disease: intra-articular fractures distort the articular surface either due to malunion or progressively from repeated subclinical fractures [6], and lax ligaments and capsules resulting from repetitive minor trauma also damage hyaline cartilage.

King and Bobechko [7] described the most common long-bone deformities of patient with OI. These are anterior and lateral bowing of the femur, which occurs in 86%, 82% and 50% of patients with congenital, tarda-I and tarda-II forms of OI, respectively, and anterior bowing of the tibia, which occurs in 86% 73% and 46%, respectively, of such patients. The most severe deformities arise in the tibia. Genu valgum occurs in 27% and 14% of patients with tarda-I and tarda-II forms, respectively. The high rates of femur and tibia deformities comprise major problem. Extra-articular deformity requires extra- or intra-articular osteotomy. To correct a severe extra-articular deformity by combining intra-articular bone resection with soft-tissue balancing is technically difficult. Some authors

have recommend corrective osteotomy before total knee arthroplasty if the deformity is >15° in the proximal part of the tibia or the distal part of the femur [8,9]. However, this requires staged operations, and nonunion might result at the osteotomy site. Our patient refused to undergo staged operations because he wished to return to work as soon as possible. In addition, the preoperative mechanical axis ran near the center of the knee, indicating that joint alignment was not necessary. Because the preoperative mechanical axis was <3°, we cut the joint surfaces *in situ* and decided to proceed with one-stage total knee arthroplasty.

In general, the most obvious features of an osteoarthritic joint are damaged cartilage and alterations in the shape of the articular surfaces. Subchondral bone in weight-bearing areas of the knee joint is usually considerably thickened. However, the subchondral bone of our patient was thin and he had few trabeculae, which were abnormally thin because of OI. Bone in patients with OI is less dense and smaller than normal bone because of sluggish periosteal bone formation [1]. Trabeculae are less numerous and abnormally thin. Although individual osteoblasts produce less bone than normal, the overall bone formation rate in the trabecular compartment is amplified because of excess osteoblasts. However, this increase in osteoblasts does not cause a net gain in trabecular bone mass, because bone resorption activity is also enhanced. The strength of the trabecular bone at the proximal tibia is regarded as a crucial factor in achieving stable fixation of the tibial component in TKA [10,11]. Ming et al. [12] showed that the implant tilted more in uncemented fixation when preoperative BMD was low, but not obviously in cemented fixation. Some authors have suggested that osteopenia should be a relative contraindication to cementless arthroplasty because of decreased ability to support the tibial component [13]. We therefore proceeded with cemented TKA for this patient.

Osteopenia associated with qualitative defects of the bone matrix is probably responsible for the high fracture rate in children with OI [14]. Although the fracture rate decreases with age [2,7], bone mineral density (BMD) usually remains low in adults with OI. Osteopenia is the most important risk factor for periprosthetic fracture after TKA [15,16]. Cyclical intravenous pamidronate effectively treats bone fragility in children with OI [17], and intravenous pamidronate prevents fragile fractures without inhibiting bone growth. Iwamoto et al. [14] showed that etidronate combined with alfacalcidol reduces urinary NTx levels, resulting in increased lumbar BMD and back pain relief among adult patients. They concluded that alendronate, which is now available in Japan, seems to engender a better response to osteoporosis than etidronate. Therefore, we administered alendronate combined with alfacalcidol.

This experience highlighted some potential pitfalls that should be considered when planning and performing TKA for patients with OI.

Although the possibility of periprosthetic fracture is a concern, we believe that total knee arthroplasty can be appropriate treatment for osteoarthritis in patients with OI. To our knowledge, only three knees have been replaced in patients with OI [3] and these also used cemented TKA and a small implant. The surgical procedures applied to these patients were not discussed in detail but severe extra-articular deformities were not evident on X-rays. Thus, the surgical procedure might have been conventional. However, our patient had a severe extra-articular deformity, but the mechanical axis ran near the center of the knee and required less soft tissue release. The aggressive release of soft tissue would have resulted in difficulties associated with controlling the soft tissue balance because of the OI. Our patient was satisfied with the short-term surgical outcome. Even when an extra-articular deformity is severe, TKA is a beneficial strategy for treating knee osteoarthritis with OI if the mechanical axis runs near the center of the knee. However, long-term follow-up should consider prosthetic loosening, sinking, and periprosthetic fracture.

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ORIGINAL ARTICLE

Elevated levels of soluble fibrin in patients with venous thromboembolism

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Abstract The fibrin-related markers (FRMs), including soluble fibrin (SF), D-dimer and fibrin and fibrinogen degradation products (FDP) are considered to be useful for the diagnosis of thrombosis; however, evidence for the diagnosis of thrombosis by SF is still not well established. The present study was designed to evaluate the usefulness of SF in the diagnosis of venous thromboembolism (VTE). The plasma concentrations of FRMs were measured in 551 inpatients suspected to have a VTE. The plasma levels of SF, D-dimer and FDP were significantly higher in patients with VTE than patients without VTE and those were significantly higher in patients without VTE than in healthy volunteers. In a receiver operating characteristic analysis for the diagnosis of VTE, the area under the curve was 0.950 for SF, 0.933 for FDP and 0.805 for D-dimer. The appropriate cut-off values for the diagnosis were as follows SF 5.9 μg/ml, FDP 2.1 μg/ml and D-dimer 4.8 μg/ml. To obtain a 100% negative predictive value for the diagnosis of VTE, the SF was less than 5.2 μg/ml, FDP was less than 1.3 μg/ml, and D-dimer was less than 0.5 μg/ml. Our findings suggest that the SF assay is useful for the diagnosis and exclusion of VTE.

Keywords SF · D-dimer · FDP · VTE · Diagnosis

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1 Introduction

The fibrin-related markers (FRMs) which include fibrin and fibrinogen degradation products (FDP), soluble fibrin (SF) and D-dimer, are sensitive markers for thrombotic diseases [1, 2]. The FRMs are reported to be elevated in deep vein thrombosis (DVT)/pulmonary embolism (PE) [3–5], disseminated intravascular coagulation (DIC) [6–8], acute myocardial infarction (AMI) [9, 10] and thrombotic thrombocytopenic purpura (TTP) [11]. The International Society of Thrombosis and Haemostasis (ISTH) established the diagnostic criteria for overt-DIC using FRM [12]. PE is a common, frequently undiagnosed, and potentially fatal event. Because the symptoms of PE are common, including dyspnoea and chest pain [13–15], the early recognition of DVT [16] and PE [17] by FRM is important clinically.

FDP is the most classical and basic marker of FRM, but the use of FDP is less common than that of D-dimer. D-

dimer is widely used to diagnose thrombosis as DVT but many of the commercially available D-dimer assay kits contain different monoclonal antibodies and standard substances, and are based on different assay systems. Since the issue of the standardization of D-dimer assays remains to be resolved, several studies [18, 19] have reported the basic data for the standardization of D-dimer.

The presence of soluble fibrin (SF) [20] in plasma is an indicator of thrombin activation in the blood, as are the thrombin–antithrombin complex [21] and prothrombin fragment F1 + 2 [21]. Thrombin cleaves fibrinopeptide A and B from the Aα and Bβ chains of fibrinogen, respectively. These are called desAA-fibrin monomer (FM) and desAABB-FM, which polymerize with each other and forms fibrin clots. These molecules in soluble form circulate in the blood are termed as SF. SF mainly consists of desAA-FM or desAABB-FM, which forms a complex with fibrinogen or its derivates [22–24]. Recently, the monoclonal antibody J2–23, which recognizes the epitope within the Aα502–521 region of fibrinogen, was developed for measuring the SF level[25].

The present study was designed to evaluate the usefulness of the SF assay in the diagnosis of thrombosis, such as DVT and PE. For this purpose, we determined the plasma concentration of these molecules in 551 patients suspected of a having venous thromboembolism and 99 healthy volunteers (HV).

2 Materials and methods

2.1 Subjects

From 1 January 2004 to 31 December 2007, 551 patients (median 25–75%) (63, 48–72 years of age; 325 females and 226 males) were suspected of having thrombosis in the hospitals affiliated with Mie University Graduate School of Medicine. The plasma concentrations of fibrin and fibrinogen degradation products (FDP), SF and D-dimer and were examined in these patients and correlated with thrombosis. The study protocol was approved by the Human Ethics Review Committees of the participating institutions and a signed consent form was obtained from each subject. Among these patients, 484 patients (62, 47–71 of age; 278 females and 206 males) did not have any thrombosis, 67 patients had a VTE (DVT or PE) (67, 54–74 years of age; 47 females and 20 males). DVT was diagnosed by either echo or venography and PE was diagnosed by computed tomography, angiography or ventilation-perfusion lung scan.

Among the underlying diseases in these patients, orthopaedic conditions were identified in 117 patients, cancer in 102, cardiovascular diseases in 83, haematological diseases in 55, digestive diseases in 31, autoimmune diseases in 28, respiratory diseases in 21, thrombophilia in 15, no underlying disease in 14, infectious diseases in 10, trauma and burn in 8, and other diseases in 7 (Table 1).

Citrated blood samples were obtained from the peripheral veins of healthy subjects (see below) and patients under fasting conditions and then centrifuged for 20 min at 3,000 rpm. The supernatants (plasma) were analyzed within 4 h. The plasma concentrations of SF and D-dimer were measured in patients with thrombosis at the onset and those without thrombosis at the first consultation. The same parameters were also measured in 99 healthy subjects (mean age 22 years, range 21–30 years; 41 females and 58 males), who were free of any diseases including thrombotic disease or hyperlipidemia as confirmed by an annual medical check-up.

Table 1 Underlying diseases of the subjects

Diseases	Age; median (25th–75th percentile)	Sex (F:M)	DVT (%)
Orthopaedic diseases	61 (34–73)	121:56	24 (13.6)
Cancer	65 (53–74)	42:60	6 (5.9)
Cardiovascular diseases	66 (50–72)	49:34	11 (13.3)
Hematological diseases	59 (36–68)	29:26	1 (1.8)
Digestive diseases	61 (34–73)	15:16	4 (12.9)
Autoimmune diseases	57 (52–63)	23:5	3 (10.7)
Respiratory diseases	62 (43–72)	12:9	0
Thrombophilia	42 (30–60)	12:3	4 (26.7)
No underlying disease	67 (53–76)	10:4	14 (100)
Infectious diseases	65 (49–72)	4:6	0
Trauma/burn	36 (18–60)	3:5	0
Other diseases	36 (32–55)	5:2	0

2.2 Measurement of plasma concentrations of SF, D-dimer and FDP

The plasma levels of SF were determined by the latex agglutination method using Nanopia SF (SEKISUI MEDICAL CO. LTD. Tokyo, Japan) containing monoclonal antibody J2–23 [25]. J2–23 recognizes an epitope in the C-terminal region of the fibrin Aα chain (Aα502–521). The plasma D-dimer and FDP levels were measured by the latex agglutination method using the Nanopia D-dimer and Nanopia P-FDP kits (SEKISUI MEDICAL CO. LTD).

2.3 Statistical analysis

The data are expressed as the median (25–75th% percentile). Differences between the groups were examined for statistical significance using the Mann–Whitney U test while correlations between two variables were tested by Pearson's correlation analysis. P value less than 0.05 denoted a significant difference. The usefulness of D-dimer levels in the diagnosis of thrombosis and VTE was examined by receiver operating characteristic (ROC) analysis [26]. The cut-off values were determined by ROC analysis. All statistical analyses were performed using the SPSS II software package (SPSS Japan, Tokyo).

3 Results

The plasma concentrations of SF were not distributed normally among healthy volunteers; the 95% confidence interval (CI) of SF was from 0 to 5.47 μg/ml. The 95% CIs of D-dimer and FDP in healthy volunteers were from 0.4 to 1.2 μg/ml and from 0.3 to 2.1 μg/ml, respectively. The plasma levels of SF tended to be high in all subjects, especially in those with infectious diseases, those with trauma and burn and those without underlying disease. The plasma levels of D-dimer tended to be high in those with orthopaedic conditions and those without underlying disease, and those of FDP tended to be high in those with infectious diseases and those without underlying disease (Table 2).

The plasma levels of SF were significantly higher in patients with VTE (22.1, 11.4–38.3 μg/ml) than patients without VTE (3.4, 1.9–5.5 μg/ml) and those were significantly higher in those without VTE than in HV ($P < 0.001$, respectively; Fig. 1). The plasma levels of D-dimer were significantly higher in patients with VTE (1.8, 1.0–5.3 μg/ml) than patients without VTE (0.8, 0.5–1.4 μg/l) and those were significantly higher in those without VTE than in HV (0.5, 0.5–0.6 μg/ml) ($P < 0.001$, respectively; Fig. 2). The plasma levels of FDP were significantly higher in patients with VTE (12.2, 7.2–20.8 μg/ml) than patients without VTE (1.4, 0.8–3.5 μg/ml) and those were significantly higher in those without VTE than in HV (0.7, 0.5–1.0 μg/ml) ($P < 0.001$, respectively; Fig. 3).

The relationship between SF and FDP ($Y = 3.804 + 0.911X$, $r = 0.553$) and that between SF and D-dimer ($Y = 5.599 + 0.542X$, $r = 0.543$) were moderately close, and the relationship between FDP and D-dimer ($Y = 2.204 + 0.549X$, $r = 0.905$) was markedly close.

In the ROC analysis for the diagnosis of VTE, the 3 curves of SF, D-dimer and FDP showed convexity at the top. The area under the curve (AUC) was 0.950 in SF, 0.933 in FDP and 0.805 in D-dimer (Fig. 4). The appropriate cut-off values for the diagnosis were as follow: SF 5.9 μg/ml [sensitivity 98.5%, specificity 80.1%, positive predictive value (PPV) 36.3%, negative predictive value (NPV) 99.8% and odds ratio 265.7], FDP 2.1 μg/ml (sensitivity 98.6%, specificity 68.1%, PPV 26.2%, NPV 99.7% and odds ratio 140.9), D-dimer 4.8 μg/ml (sensitivity 28.4%, specificity 96.6%, PPV 48.7%, NPV 92.1% and odds ratio 11.1) (Table 3). In 100% of NPV for the diagnosis of VTE, SF was less than 5.2 μg/ml, FDP was less

Table 2 Plasma levels of SF, D-dimer and FDP in the underlying diseases of the subjects

Diseases	SF (μg/ml)	D-Dimer (μg/ml)	FDP (μg/ml)
Orthopaedic diseases	3.8 (2.4–8.0)	4.9 (1.9–12.9)	0.9 (0.6–1.7)
Cancer	3.4 (1.8–6.2)	0.9 (0.7–1.4)	1.5 (0.9–3.2)
Cardiovascular diseases	3.9 (2.2–10.6)	1.1 (0.5–2.0)	2.2 (0.8–7.5)
Hematological diseases	2.6 (1.2–5.5)	0.7 (0.4–1.2)	1.0 (0.7–2.0)
Digestive diseases	4.4 (2.0–8.4)	0.9 (0.6–1.6)	1.3 (0.8–3.9)
Autoimmune diseases	3.1 (1.7–4.8)	0.6 (0.4–0.9)	1.2 (0.7–3.1)
Respiratory diseases	2.5 (1.0–4.8)	0.6 (0.5–0.9)	1.1 (0.7–1.3)
Thrombophilia	3.8 (1.7–9.4)	0.5 (0.4–1.0)	1.4 (0.7–3.2)
No underlying disease	23.6 (7.0–32.0)	2.1 (1.0–5.3)	10.2 (5.0–19.9)
Infectious diseases	5.8 (1.5–18.3)	1.2 (0.9–2.7)	4.3 (1.8–6.9)
Trauma/burn	10.4 (1.8–12.0)	0.9 (0.7–1.4)	3.4 (1.4–5.6)
Other diseases	2.1 (0.0–4.7)	0.9 (0.6–1.9)	1.5 (1.4–4.1)

Data show the median (25–75%) percentile

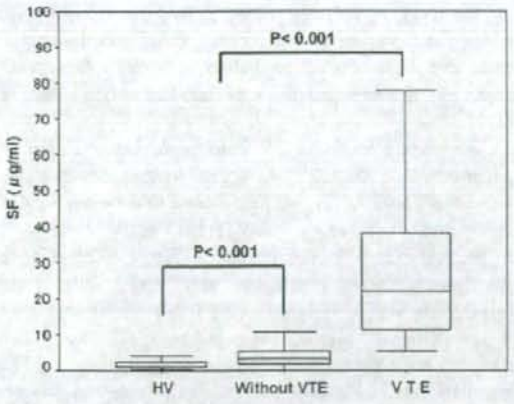

Fig. 1 Plasma concentrations of SF in patients without VTE, those with VTE and healthy volunteers. *VTE* venous thromboembolism, *HV* healthy volunteer

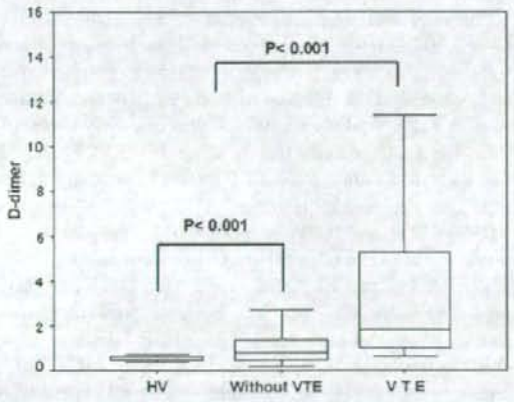

Fig. 2 Plasma concentrations of D-dimer in patients without VTE, those with VTE and healthy volunteers *VTE* venous thromboembolism, *HV* healthy volunteer

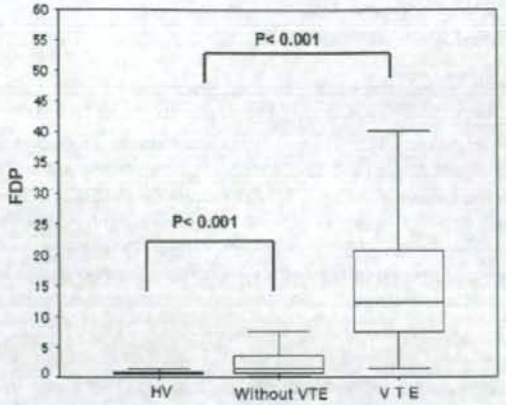

Fig. 3 Plasma concentrations of SF in patients without VTE, those with VTE and healthy volunteers *VTE* venous thromboembolism, *HV* healthy volunteer

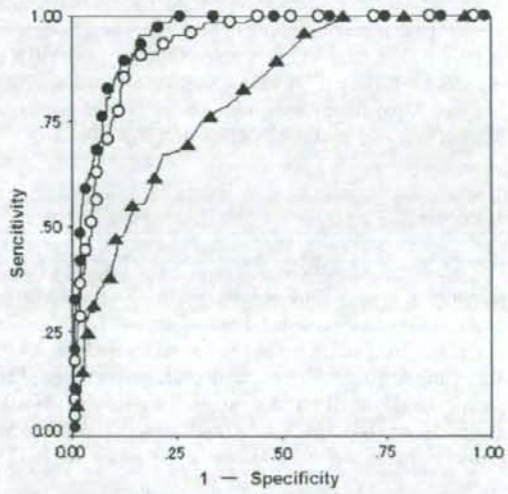

Fig. 4 ROC analysis for diagnosis of VTE. *Closed circle* SF, *open circle* FDP, *closed triangle* D-dimer AUC SF 0.950, FDP 0.933, D-dimer 0.805

than 1.3 μg/ml, and D-dimer was less than 0.5 μg/ml (Fig. 5).

4 Discussion

In the present study, the normal SF level was less than 6.0 μg/ml, and that was similar to the previous reports for other kinds of SF determination [22, 24]. The monoclonal antibodies in the Nanopia SF [25], Iatro SF [24] and Auto LIA FMC [27] assays recognize the α-chain of fibrinogen, which is an important site for the activation of fibrinogen to fibrin by thrombin. The normal range of D-dimer and FDP were from 0.4 to 1.2 μg/ml and from 0.3 to 2.1 μg/ml, respectively. These findings are in agreement with those of previous reports [2, 28].

The plasma levels of SF, D-dimer and FDP were significantly higher in patients with VTE than patients without VTE, suggesting that these FRMs were useful for the diagnosis of VTE. In previous reports [2, 28, 29], the high concentrations of SF and D-dimer could be considered as markers of thrombosis, including VTE. However, no significant difference was observed among those with thrombosis, those with liver transplantation or those with a post operative status [2].

Table 3 Appopriate cut-off value of SF, D-dimer and FDP for the diagnosis of VTE

Marker	Cut off value (μg/ml)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Odds ratio
Highest odds ratio						
SF	5.9	98.5	80.1	36.3	99.8	265.7
D-Dimer	4.8	28.4	96.6	48.7	92.1	11.1
FDP	2.1	98.5	68.1	26.2	99.7	140.9
Highest NPV (100%)						
SF	5.2	100	76.0	32.4	100	
D-Dimer	0.5	100	34.3	14.9	100	
FDP	1.3	100	56.1	20.7	100	

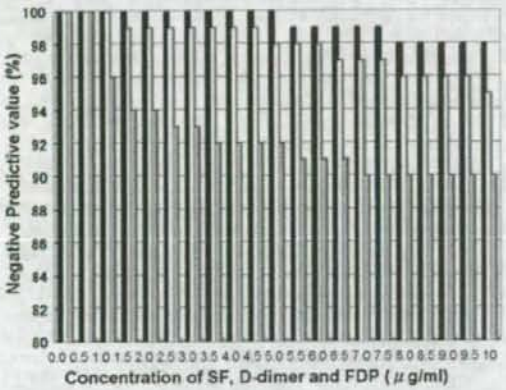

Fig. 5 Negative predictive value for the diagnosis of VTE. *Closed bar* SF, *shaded bar* D-dimer, *open bar* FDP

The plasma levels of SF tended to be high in all subjects, especially those with infectious diseases, those with trauma and burn and those without underlying disease, suggesting that these diseases have a hypercoagulable state or thrombosis. The plasma levels of D-dimer also tended to be high in those with orthopaedic conditions and those without underlying disease, indicating that D-dimer levels might be high in orthopaedic conditions without thrombosis, and that D-dimer may therefore not be useful for the diagnosis of thrombosis under those conditions.

The ROC analysis showed that SF, FDP and D-dimer are useful markers for the diagnosis of VTE; in particular, SF was the best marker of the FRMs. An appropriate cut-off value for the diagnosis of VTE was 5.9 μg/ml in SF, 2.1 μg/ml in FDP and 4.8 μg/ml in D-dimer. Except in the D-dimer, these cut-off values were close to the normal range and a slight increase of the SF and FDP from the normal range shows a high risk of thrombosis. At a value of 5.9 μg/ml for SF, both the sensitivity and specificity were sufficiently high, thus suggesting that SF is the best marker for the diagnosis of thrombosis at the onset. At the value of 4.8 μg/ml for D-dimer, the specificity was highest, suggesting that the diagnosis of VTE might be confirmed by high D-dimer levels.

In 100% of NPV for the diagnosis of VTE, SF was less than 5.2 μg/ml, FDP was less than 1.3 μg/ml and D-dimer was less than 0.5 μg/ml. In Europe and North America, D-dimer concentrations of less than 0.5 μg/ml are considered to exclude DVT/PE [17]. However, some D-dimer kits, which are frequently used in Japan have different cut-off values for the exclusion of DVT/PE [28]. These findings for D-dimer were similar to previous reports [28]. However, this study is the first to show that the SF level is a valuable indicator for the exclusion of DVT/PE.

Finally, the FRMs such as D-dimer, FDP and SF are considered to be useful for the diagnosis of thrombosis, and the SF level reflects the early phase of DVT/PE while D-dimer reflects the secondary fibrinolysis after clot formation [2]. By establishing an early diagnosis of thrombosis by FRM, we might improve the outcome in various underlying diseases, which carry a risk for the development of thrombosis.

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Original article

Prevalence and risk factors for knee osteoarthritis in elderly Japanese men and women

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Abstract

Background. The aims of the present study were to examine the prevalence and risk factors for knee osteoarthritis in elderly Japanese men and women.

Methods. We examined 598 of the 1513 inhabitants of Miyagawa village aged ≥ 65 years (393 women, 205 men). Baseline data, obtained with standard questionnaires, included information on age, past history, sports activity, working, knee pain, smoking, and intakes of alcohol and milk. Bone mineral density of the forearm was measured using dual energy X-ray absorptiometry. Anteroposterior radiographs of both knees were graded for osteoarthritis using the Kellgren-Lawrence grading system. Definite osteoarthritis was defined as a grade of 2 or higher. We used logistic regression analysis by the stepwise method to determine the risk factors for radiographic knee osteoarthritis.

Results. The prevalence of definite radiographic knee osteoarthritis was 30.0% overall: 17.7% in men and 36.5% in women. The prevalence of symptomatic knee osteoarthritis was 21.2% overall: 10.7% in men and 26.7% in women. There were significant differences in the risk of radiographic knee osteoarthritis with body mass index (BMI), sex, age, and bone mineral density (BMD).

Conclusions. The prevalence of definite radiographic knee osteoarthritis was 30.0% and that of symptomatic knee osteoarthritis was 21.2%. We found that higher BMI, female sex, older age, and higher BMD were significantly associated with an increased risk for radiographic knee osteoarthritis.

Introduction

It is well known that Japan is one of the major aging societies in the world. In the elderly, knee osteoarthritis (OA), the most common joint disorder, is an important cause of impairment and disability with associated costs of health care. If risk factors of knee OA could be identified, there is the potential to decrease disability and related health care expenses substantially. Many risk factors and their association with knee OA have been reported in several studies.[1–3] Well-recognized factors associated with knee OA include being female[4] and the effects of obesity[1,2] and age.[5,6] However, it is controversial whether knee OA is associated with higher bone mass.[7–10] Moreover, few studies have been performed regarding the prevalence and risk factors for knee OA in elderly Japanese men and women.[1]

We report herein an epidemiological study on the prevalence and risk factors of knee OA in elderly Japanese men and women.

Materials and methods

We recruited community inhabitants at least 65 years of age living in a typical mountain village, Miyagawa, in central Mie Prefecture, Japan. A total of 1513 persons in this village met the age criterion, among whom 598 inhabitants (39.5% of the inhabitants) participated in this study. These 393 women and 205 men ranged in age from 65 to 98 years and had an overall mean age of 73.6 years (73.7 years for women, 73.5 years for men). The baseline examination was performed at the Houtoku Hospital in the village. The Committee on the Ethics of Human Research of our hospital approved the study protocol, and informed consent was obtained from all participants.

The baseline data, obtained with standard questionnaires administered by orthopedic surgeons, included information on age, past history, sports activity (like or dislike), working history (white-collar or blue-collar job), knee pain, smoking, and intakes of alcohol and milk. The items of the past history specifically asked about were fractures, operations (gastrectomy, among others), knee trauma, osteoporosis, diabetes mellitus, and gout. In women, age at menopause and past history

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of ovariectomy were also investigated. Anthropometric measurements were made of the height and body weight. The body mass index (BMI) was calculated as the weight in kilograms divided by the square of the height in meters. Other medical examinations were radiographs of the knee joints and bone mineral density (BMD). The BMD of the forearm was measured using dual energy X-ray absorptiometry (DCS-600EX; Aloka, Tokyo, Japan).

Anteroposterior radiographs of both knees were graded for radiographic knee OA using the Kellgren-Lawrence grading system.[11] This system uses the following grades: grade 0, normal; grade 1, possible osteophytes only; grade 2, definite osteophytes and possible joint space narrowing; grade 3, moderate osteophytes and/or definite joint space narrowing; and grade 4, large osteophytes, severe joint space narrowing, and/or bony sclerosis. Definite radiographic knee OA was defined as a Kellgren-Lawrence grade of 2 or higher, and the final grade assigned to a subject's radiograph was the highest grade for the most severely affected knee. All knee radiographs were evaluated by three trained orthopedists independently. The final score was that which was agreed upon by two or three orthopedists; but when differences occurred among the three orthopedists, the middle score was accepted. Symptomatic knee OA was defined as definite radiographic knee OA with knee pain.

Differences in the baseline characteristics by OA status were analyzed by *t*-test for continuous variables and by χ^2 test for discrete variables. The Cochran-Armitage trend test was used to evaluate the correlations between the prevalence of each definite radiographic knee OA and age group. Moreover, we performed stepwise forward logistic regression analysis to identify the risk factors on definite radiographic knee OA. Variables considered in the analysis were age, BMI, BMD, sex, fractures, operations, knee trauma, osteoporosis, diabetes mellitus, gout, sports activity, working, smoking, and intakes of alcohol and milk. Category data were divided into two or three groups, as shown in Table 2 (see below); and age, BMI, and BMD were treated as continuous variables. The significance level for entry into the model was 0.05.

Results

Table 1 shows the distribution of Kellgren-Lawrence grades and the average patient age for each grade. The prevalence of definite radiographic knee OA was 30.0% overall; 17.7% in men and 36.5% in women.

Figure 1 shows the prevalence of radiographic knee OA by age and sex grouping. In both sexes, the prevalence continued to increase with age but not significantly (men, $P = 0.052$; women, $P = 0.056$ by the

Table 1. Frequency distribution of Kellgren-Lawrence grades and average age

Patients	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Total	37.6% (72.9)	32.1% (73.3)	16.1% (73.5)	9.7% (75.3)	4.2% (78.1)
Women	35.4% (73.2)	28.1% (73.2)	19.9% (73.1)	11.5% (75.4)	5.1% (79.0)
Men	42.2% (72.5)	40.0% (73.6)	8.8% (75.4)	6.4% (75.3)	2.5% (74.4)

Numbers in parentheses indicate the average age

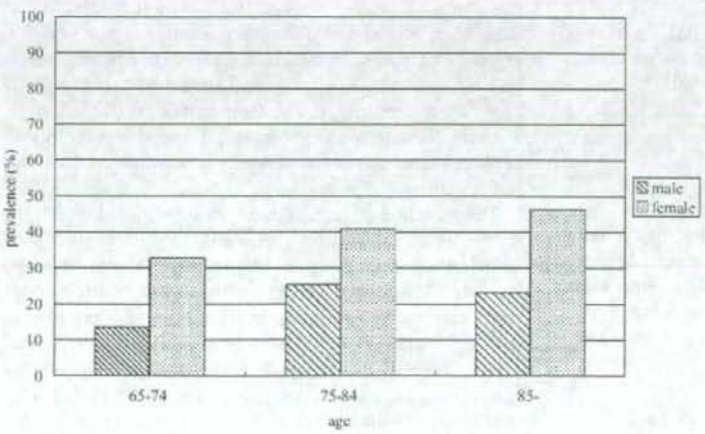

Fig. 1. Prevalence of radiographic knee osteoarthritis (OA) by age and sex group