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ORIGINAL ARTICLE

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Long-term outcome of patients with rheumatoid arthritis treated by multiple arthroplasty

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Abstract We conducted a study of 82 patients with rheumatoid arthritis (RA) who had undergone multiple arthroplasty and investigated their clinical findings and clinical courses. We reviewed the significance of multiple arthroplasty in the treatment of RA, its problems, and measures to solve them. All patients initially regained and maintained good walking capacity. However, the walking capacity of many patients again decreased over the long term; in the tenth year, 79% of patients were capable of a practical gait. The causes of decreased walking capacity included complications of artificial joints, cervical lesions, and vertebral compression fractures. Fractures were observed in as many as nine patients, indicating that it is important to prevent and treat their cause, that is, osteoporosis. The survival rate was 71% in 10 years. In RA patients, particularly those who have undergone multiple arthroplasty, the major causes of death are infection and rheumatic disease, suggesting that prevention of such diseases should be considered paramount. Appropriate systemic treatment of RA, patient education, and measures against osteoporosis for prevention of complications may preserve the worth of multiple arthroplasty for RA patients with multiple joint destruction.

Key words Multiple arthroplasty · Rheumatoid arthritis (RA) · Survival analysis · Walking ability outcome

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Introduction

Rheumatoid arthritis (RA) begins with chronic multiple arthritis and progresses to multiple joint destruction. RA treatment with biological products is advancing, but it has not yet led to appreciable changes in the natural course of RA.[1] In particular, in many cases of the more erosive subset of rheumatoid arthritis and in mutilans-type rheumatoid arthritis,[2] destruction of joints, including large joints such as the hip and knee, progresses and results in impairment of the activities of daily living (ADL), especially walking capacity. Arthroplasty for patients with joint destruction is valuable as a means to regain and maintain ADL, especially practical walking capacity, and to improve the quality of life (QOL), as well as to repair joint function. Arthroplasty plays an important part in the treatment of advanced RA, along with drug therapy and rehabilitation. On the other hand, problems and complications are unusual. Particularly in patients who have undergone multiple arthroplasty, their functional and vital prognosis should be taken into consideration with respect to the problems associated with artificial joints. We investigated the long-term treatment outcome and prognosis in RA patients who had undergone multiple arthroplasty and reviewed the significance and problems of the procedure, and measures available to treat those problems.

Materials and methods

Typically, patients who have undergone surgery for three or more hip or knee joints are regarded as multiple arthroplasty patients.[3,4] A total of 87 multiple arthroplasty patients with RA underwent their first surgery during the 20 years between April 1980 and March 2000. Among them, 82 patients were included in this study, excluding five patients lost to follow-up owing to such causes as changes of address. The mean age at the first surgery was 57.6 years (34–81 years old), and the patients comprised one man and 81

women. The mean duration of disease was 19.3 years (5–42 years). Based on the wrist joint radiographic stage, all patients except for four, who were in Steinbrocker stage II, had late-stage RA; 37 were in stage III, 18 in stage IV, and 23 had mutilans-type rheumatoid arthritis stage III-c[2], which is demonstrated by melting and elimination of the carpal bone. Forty-eight patients underwent four-joint replacement, that is, bilateral total hip arthroplasty (THA) and bilateral total knee arthroplasty (TKA), three underwent bilateral THA and unilateral TKA, and 31 underwent unilateral THA and bilateral TKA. For patients who had died, the findings prior to onset of the complications causing death were used in this study. The duration of the postoperative course, from the first surgery to the time of the study, ranged from 4 to 24 years, and the mean duration was 8 years 9 months.

We investigated the clinical findings of the patients, clinical courses to multiple arthroplasty, causes of the worsening of the functional vital prognosis, and causes worsening the prognosis. For ADL, a modified Steinbrocker classification[5] system, which segmentalized the Steinbrocker stages, was utilized: Class 3-c patients were regarded as capable of walking outdoors with a stick; class 3-d as capable of walking practically, but only indoors; class 4-a as capable of walking for only a few steps; class 4-b as capable of standing up and moving in a wheelchair; class 4-c as capable of sitting only on the bed; and class 4-d as bedridden and incapable of remaining in a sitting position.

Results

Clinical findings

Many patients had persistent high RA activity despite multiple arthroplasty, with a high inflammatory reaction as indicated by C-reactive protein (CRP) levels: mean, 2.3 mg/dl (0.6–5.6 mg/dl). The mean rheumatoid factor was high at 98.2 IU/ml, and only four patients were seronegative (below 15 IU/ml). All patients were resistant to multiple disease-modifying antirheumatic drugs (DMARDs), and 42 patients (51%) received methotrexate at the time of the study, whereas 54 (66%) required concomitant use of prednisolone at a mean daily dose of 6.3 mg (4–15 mg). Most of the patients showed progression of the wrist joint radiographic stage even after the first surgery; four patients progressed to stage III, 25 to stage IV, and 53 (65%) progressed to stage III-c mutilans-type rheumatoid arthritis.

Course to multiple arthroplasty

The patients were classified into three groups based on their courses to multiple arthroplasty. Group 1 comprised 22 patients who had already been found to have multiple joint destruction at the first visit and who underwent multiple arthroplasty involving the simultaneous replacement of two joints. Group 2 comprised 18 patients with low walking capacity prior to their first surgery who experienced progressive hip joint destruction within 1 year after the first surgery, mainly bilateral TKA, and underwent multiple arthroplasty. Group 3 comprised 42 patients who experienced gradual joint destruction during long-term treatment and underwent multiple arthroplasty.

In group 1, simultaneous bilateral TKA was performed in ten patients and simultaneous THA and TKA for 13 extremities in eight patients. The mean duration from the first surgery to the last surgery was extremely short at 4 months (range, 1 month–1 year).

Case 1: A woman who was 43 years of age at the time of her first surgery had been living in a wheelchair with class 4-a disease owing to the destruction of her bilateral hip and bilateral knee joints (Fig. 1a). In May 1992, she underwent simultaneous right THA and right TKA, and 2 months later in July 1992, simultaneous left THA and left TKA. At 12 years after the surgery, she was able to easily walk outdoors and was almost independent (ADL class 2). The X-ray finding (Fig. 1b) showed no problems with any of the four artificial joints.

In group 2, simultaneous bilateral TKA was performed on 13 patients. The mean duration from the first surgery to the last surgery was 2 years and 4 months (range, 9 months–2 years 5 months).

Case 2: A 34-year-old woman with ADL class 4-b used a wheelchair for mobility owing to bilateral destruction of her knee joints (Fig. 2a). In March 2000, she underwent simultaneous bilateral TKA and became able to walk outdoors with a stick. The X-ray before TKA had shown no remarkable changes in the hip joints, but she had right coxalgia about 2 months after the surgery. Subsequently, bilateral hip joint destruction rapidly progressed (Fig. 2b) and difficulty in walking was observed. Therefore, she underwent right THA in September 2000 and left THA in October 2000. At 3 years after the surgery, she was able to easily walk outdoors with a stick (class 3-c), and the X-ray finding (Fig. 2c) showed no remarkable changes. Not a few patients experienced this so-called domino effect.[6]

In group 3, simultaneous bilateral TKA was performed on 15 patients and simultaneous THA and TKA on six patients. The mean duration from the first surgery to the last surgery was 5 years 6 months (1–12 years), indicating that patients had undergone multiple arthroplasty in the course of long-term treatment course.

Case 3: A 40-year-old woman with ADL class 3-d who had been unable to walk outdoors owing to destruction of her right hip joint (Fig. 3a) underwent right THA in March 1993 without remarkable changes in the knee joints. After the surgery, she was ADL class 2, that is, she was almost independent. Destruction of the right knee joint progressed over 6 years, and she underwent right TKA in November 1999. Destruction of the left knee joint was observed over 3 years (Fig. 3b), and she underwent left TKA in March 2003. At 11 years after the first surgery, she had undergone joint replacement surgery three times (Fig. 3c) but was able to easily walk outdoors and was almost independent with respect to ADL.

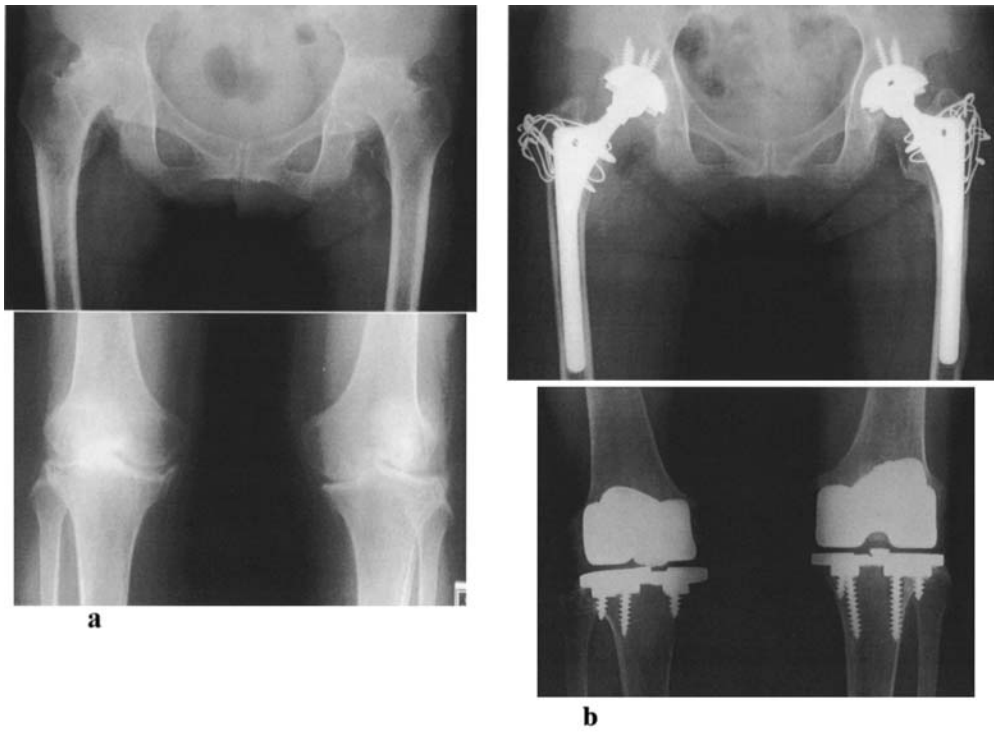

Fig. 1a,b. Case 1. **a** The X-ray finding prior to the first surgery. Marked destruction of the bilateral hip and bilateral knee joints was observed. **b** Right total hip arthroplasty (THA) using HGP2 and right total knee arthroplasty (TKA) using MG2 were simultaneously performed; left THA and left TKA were simultaneously performed 2 months later. The X-ray findings 12 years after the surgery showed no remarkable changes to the artificial joints

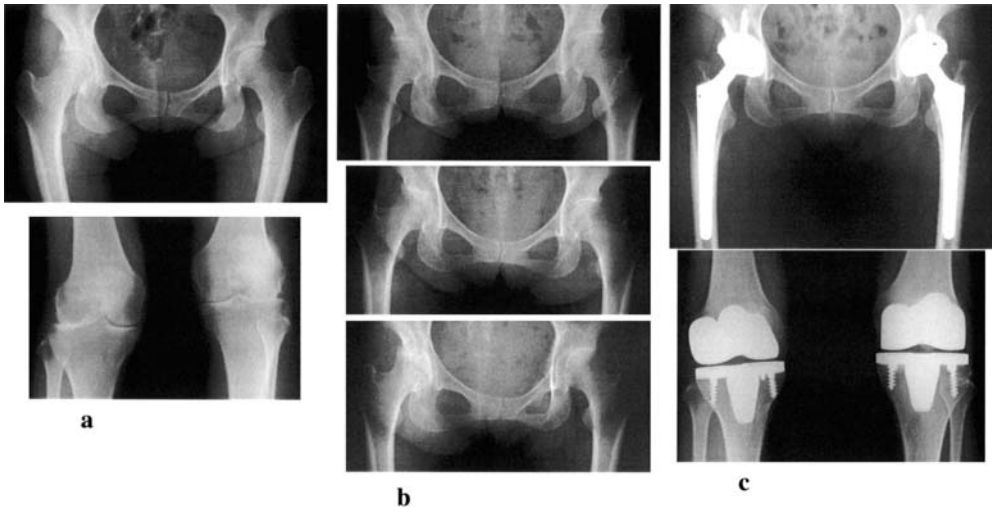

Fig. 2a–c. Case 2. **a** The X-ray finding prior to simultaneous bilateral TKA using Magna ROM21 for bilateral knee joint destruction. No remarkable changes in the hip joints were observed. **b** The destruction of bilateral hip joints rapidly progressed over the course of 2 months (*upper panel*), 4 months (*middle*), and 6 months (*lower*) after TKA. **c** Right THA using PerFix was then performed, and left THA 1 month later. The X-ray findings 3 years after the surgery showed no problems with either the bilateral THA or the bilateral TKA

Additional surgery

Various additional operations were required to maintain ADL during the treatment course. Surgery for the cervical spine is indicated for patients with a neurological deficit such as quadriplegia,[7,8] but decompression and fusion of multiple cervical vertebrae was required by eight patients. In six patients who had difficulty walking and persistent ankle pain that was resistant to conservative treatment, ankle arthroplasty was indicated[9] and performed. Bilateral total ankle arthroplasty (TAA) was performed in two patients, TAA and contralateral ankle arthrodesis in two, and

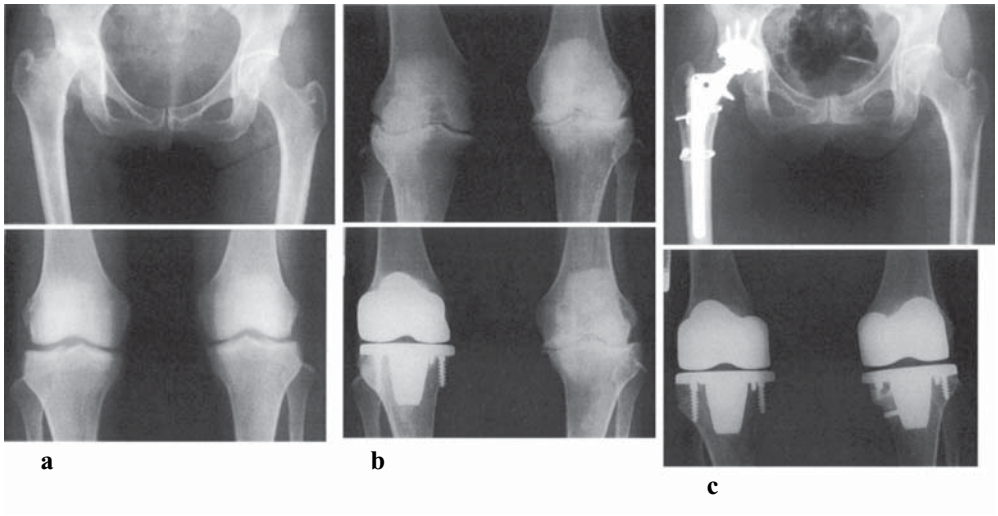

Fig. 3a–c. Case 3. **a** The X-ray finding prior to right THA using HG hybrid for right hip destruction. No remarkable changes in the knee joints were observed. **b** Right knee joint destruction progressed over 6 years (*upper*) and right TKA using Magna ROM21 was performed. Left knee joint destruction (*lower*) was observed 3 years later, and left TKA was then performed. **c** The X-ray findings 11 years after right THA, 5 years after right TKA, and 2 years after left TKA showed no remarkable changes

unilateral TAA and contralateral ankle arthrodesis in one each. Other operations were performed at the patient's request: forefoot arthroplasty in eight feet of six patients, total elbow arthroplasty (TEA) in six elbows of four patients, and wrist joint or finger arthroplasty in nine hands of eight patients. As a result, two patients underwent replacement of eight joints: bilateral THA, bilateral TKA, bilateral TAA, and bilateral TEA.

Case 4: A 55-year-old woman had been bedridden with ADL class 4-c owing to destruction of bilateral hip and bilateral knee joints (Fig. 4a). She underwent left THA in December 1992, right THA in February 1993, and simultaneous bilateral TKA in March 1993, and became able to walk outdoors. Subsequently, she was confined to walking only indoors (class 3-d) because of bilateral ankle destruction (Fig. 4b). She underwent simultaneous right ankle arthrodesis and left TAA in August 1997. At 11 years after the four-joint replacement and 7 years after the bilateral ankle surgery (Fig. 4c), she was able to easily walk outdoors with a stick (ADL class 3-c).

In the long term, complications of THA and TKA were not rare, and revision was required for 14 joints in nine patients. The causes requiring revision for THA included loosening in six hips, deep infection in one hip, and fracture in one hip, and for TKA, loosening in four knees and deep infection in two knees. In patients with artificial joint complications, except for three patients who underwent revision of THA because of fracture, revision of TKA because of loosening, and revision of TKA because deep infection, old-type implants with bone cement had been used.

Changes in ADL walking capacity and functional prognosis

Changes in ADL are shown, focusing on walking capacity, in Fig. 5. Before the first surgery, 61 patients (74%) had been incapable of walking practically (below class 4-a), and 22 (27%) had been bedridden (below class 4-c). All but three of these patients with low ADL became capable of walking practically after the first surgery. After the last surgery, all patients became capable of walking, and 59 (72%) became capable of walking outdoors (above class 3-c). However, ten patients subsequently again became incapable of walking during the long-term course, and 21 patients, including those ten, showed decreased ADL compared with that after the last surgery.

The major causes of decreased ADL included complications of the artificial joints in ten patients, cervical lesions in five, compression fracture of the thoracic or lumbar vertebrae in four, aggravated pulmonary fibrosis in one, and decreased volition with age in one. The complications of artificial joints consisted of, for THA, fracture in one patient, loosening in two, deep infection in one, and for TKA, fracture in four, loosening in one, and deep infection in one.

Case 5: A 56-year-old woman had been confined to a wheelchair with ADL class 4-b owing to destruction of the bilateral hip joints. She underwent left THA in May 1989 and right THA in April 1990, and became able to walk outdoors (ADL class 3-c). Subsequently, destruction of the knee joints progressed, and she underwent simultaneous bilateral TKA in July 1998; that is, after four joint replacements (Fig. 6a), she remained capable of walking outdoors. In November 1998, she developed quadriplegia and was diagnosed as having cervical myelopathy due to vertical subluxation, atlantoaxial subluxation, and a subaxial fibrous constricting band (Fig. 6b). She underwent decompression and spondylodesis of the occipital bone through thoracic vertebra T4 (Fig. 6c). At 6 years after the cervical surgery, she was able to walk (ADL class 3-d), but only indoors.

The time point at which patients became incapable of a practical gait was regarded as the end point, and the

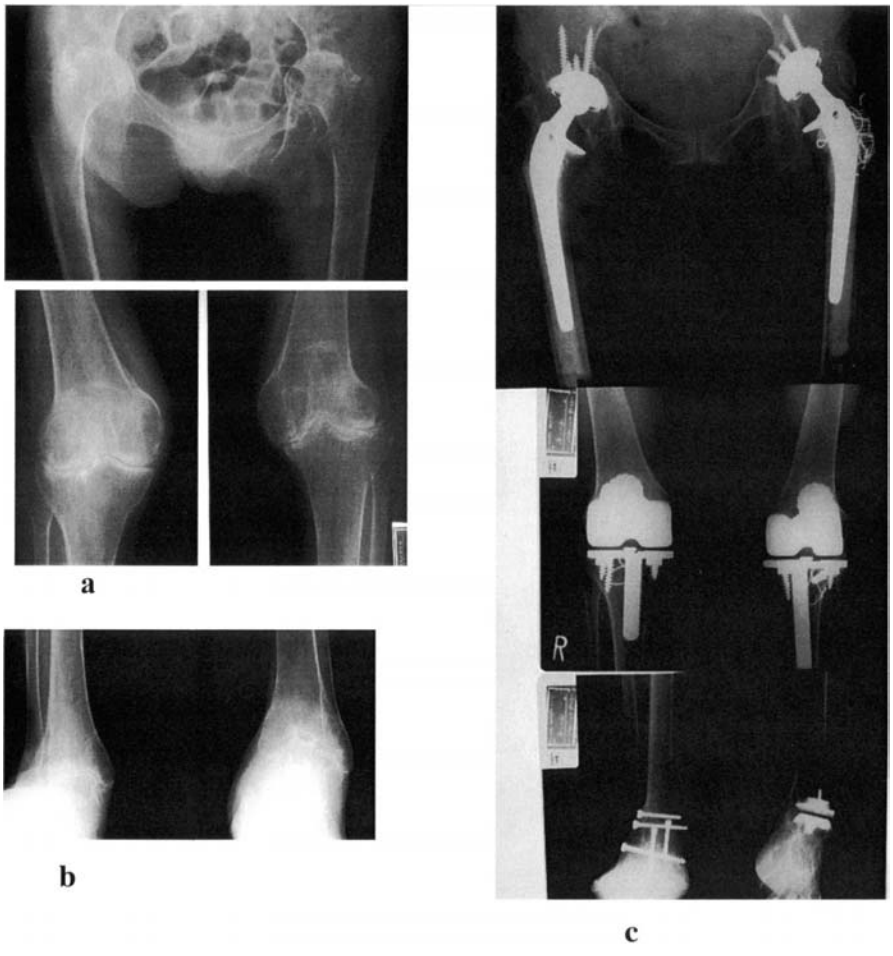

Fig. 4a–c. Case 4. **a** Severe joint destruction was observed in the bilateral hip and bilateral knee joints before surgery, and left THA using a Harris hybrid was performed, followed by right THA 2 months later, and then simultaneous bilateral TKA using a stemmed MG2 another month later. **b** Because of subsequent bilateral ankle destruction, the patient's walking was limited to indoors; thus, right ankle arthrodesis and left total ankle arthroplasty (TAA) using a Bioceram TNK type were simultaneously performed. **c** At 11 years after the four joint replacements and 7 years after bilateral ankle surgery, the X-ray showed a favorable outcome

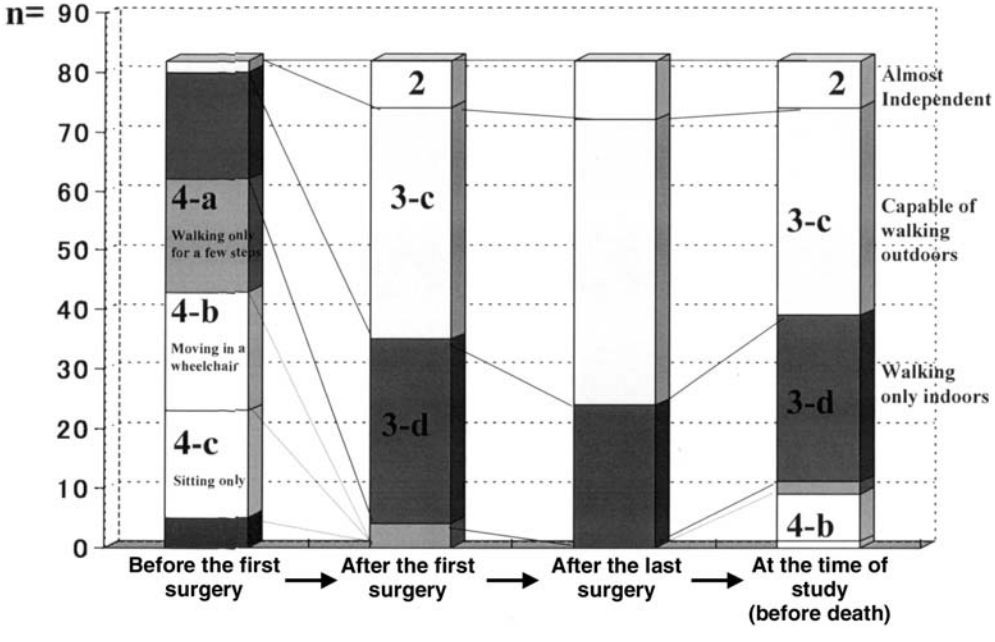

Fig. 5. Changes in activities of daily living (ADL) walking capacity. Before the first surgery, 61 patients were incapable of a practical gait and 22 had been bedridden. After the first surgery, all but three patients became capable of a practical gait, and after the last surgery, all patients became capable of walking and 59 patients were able to walk outdoors. However, ten patients again became incapable of walking during the long-term treatment course, and 21 patients showed decreased ADL

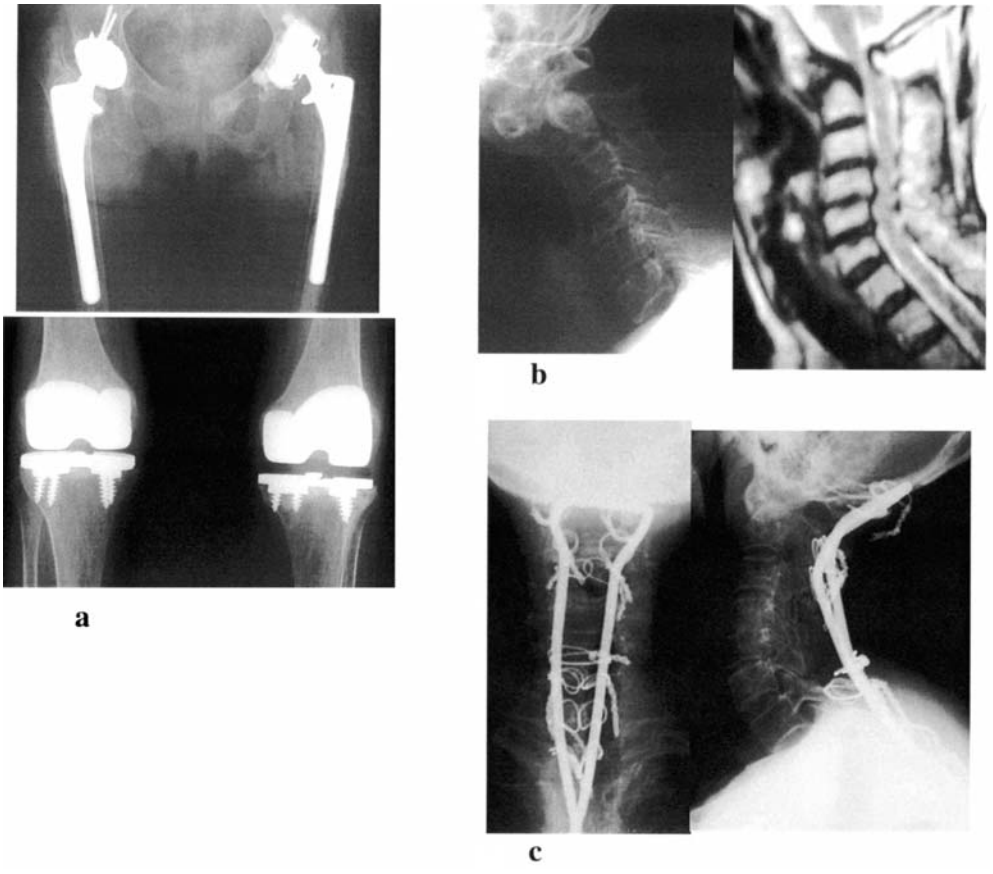

Fig. 6a–c. Case 5. **a** The patient had undergone four joint replacements (bilateral THA and bilateral TKA). **b** A plain lateral cervical X-ray (*left*) shows vertical subluxation and atlantoaxial subluxation, and a magnetic resonance image (*right*) shows subaxial spinal cord compression. **c** Decompression and spondylodesis of the occipital bone through the thoracic vertebra T4 was performed, and the X-ray image obtained 6 years after the surgery shows that the cervical vertebrae maintained stability

prognosis for long-term ADL walking capacity was determined by the Kaplan-Meier method (Fig. 7). The percentage of patients capable of walking practically with above class 3-d decreased to 92% in the 5th year after the first surgery, 79% in the 10th year, and 60% in the 15th year.

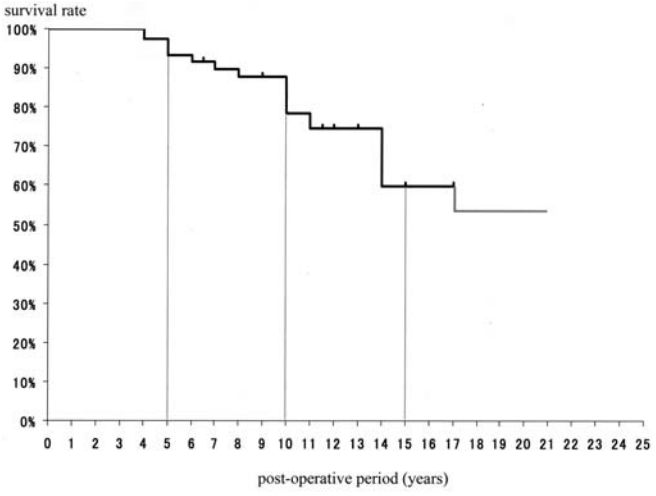

Fig. 7. Prognosis of ADL walking capacity shown by Kaplan-Meier method, in which the time point at which patients became incapable of a practical gait was regarded as the end point. Ninety-two percent of patients were capable of a practical gait in the 5th year after the first surgery, 79% in the 10th year, and 60% in the 15th year

Deaths, causes of death, and vital prognosis

At the time of the study, 28 patients (34%) had already died. The mean age at the time of death was 64.8 years (53–89 years; 1 man and 27 women). The mean time from the first surgery to death was 7 years 8 months (4–18 years). Among the patients who had died, 12 (43%) died after their ADL class had decreased to less than that after the last surgery. The most common cause of death (Table 1) was infection, in 12 patients, followed by renal failure in 8, and interstitial pneumonia in 2, indicating rheumatic disease, which is characteristic of RA. In one patient who had pneumonia and in four patients who had renal failure, concurrent amyloidosis was histopathologically confirmed. The other causes of death were cerebrovascular accident or myocardial infarction in four patients, lung cancer in one, and liver cirrhosis in one. The mean age at the time of death was 63.6 years; the youngest, for visceral organ lesions, followed by cerebral and cardiac accident, and infection. Long-term vital prognosis on the Kaplan-Meier survival curve (Fig. 8) showed that the survival rate was 90% in the 5th year after the first surgery, 71% in the 10th year, and 41% in the 15th year; the rate decreased rapidly more than 10 years after surgery.

Discussion

We conducted a study of patients with RA who had undergone multiple arthroplasty for three or more hip and knee joints to investigate their clinical findings, clinical courses, and functional and vital prognoses, and we reviewed the significance of multiple arthroplasty, its problems, and the measures used to treat them. The study included 82 patients, or 5% of all RA patients. Most of the patients were resistant to multiple DMARDs and had persistent high RA activity. Fifty-three patients (63%) were eventually diagnosed as having mutilans-type RA.[2]

The patients were classified into three groups based on their clinical courses to multiple arthroplasty. The patients in group 1 who had already presented with multiple joint destruction at their first visit might not have received appropriate treatment, including surgical therapy, previously. Since such patients are not uncommon among RA patients, the spread of medical knowledge on RA treatment is required. Surgical indication should be decided carefully in consideration of each patient's physical and psychological age and complications, but simultaneous two-joint replacement[10] was effective, particularly in patients with multiple joint destruction at the first visit, to attain practical walking capacity. Patients experiencing a possible domino effect[6] like those in group 2 are also not uncommon. In patients with poor walking capacity prior to their first surgery or with persistent high RA inflammation, early progression of hip joint destruction may occur after they have become capable of walking after TKA. Before their first surgery, such patients should be educated so they can make plans for their life in light of the possibility that they may require multiple arthroplasty. The remaining patients, those in group 3, experienced progressive joint destruction during the long-term treatment course and underwent multiple arthroplasty to maintain walking capacity. Most of those patients with the more erosive subset of RA or mutilans-type RA have such a clinical course.

After multiple arthroplasty, the patients regained and maintained a favorable ADL, especially with regard to walking capacity. However, in many patients, the ADL became lower during the long-term treatment course. In the 10th year after their first surgery, 79% of patients had a practical gait, and 60% in the 15th year. The causes of decreased walking capacity included complications of the artificial joints, compression fracture of the thoracic or lumbar vertebrae, and cervical lesions. The most common cause of decreased walking capacity was fracture, when fractures around the artificial joints were included, suggesting that prevention and treatment of osteoporosis,[11] a factor in many fractures, are essential even in patients who have undergone multiple arthroplasty. The artificial joint complications of loosening and deep infection frequently occurred in

Table 1. Cause of death ($n = 28$)

Diseases	No. of patients	Mean age at time of death in years (range)
Infection		67.1 (58–82)
Pneumonia	11[a]	
Meningitis	1	
Rheumatic disease		63.6 (53–74)
Renal failure	8[b]	
Interstitial pneumonia	2	
Cardiovascular accident		66.3 (54–69)
Cerebrovascular accident	2	
Myocardial infarction	2	
Others		78.0 (67–89)
Lung cancer	1	
Liver cirrhosis	1	

[a] Concurrent amyloidosis ($n = 1$)
[b] Concurrent amyloidosis ($n = 4$)

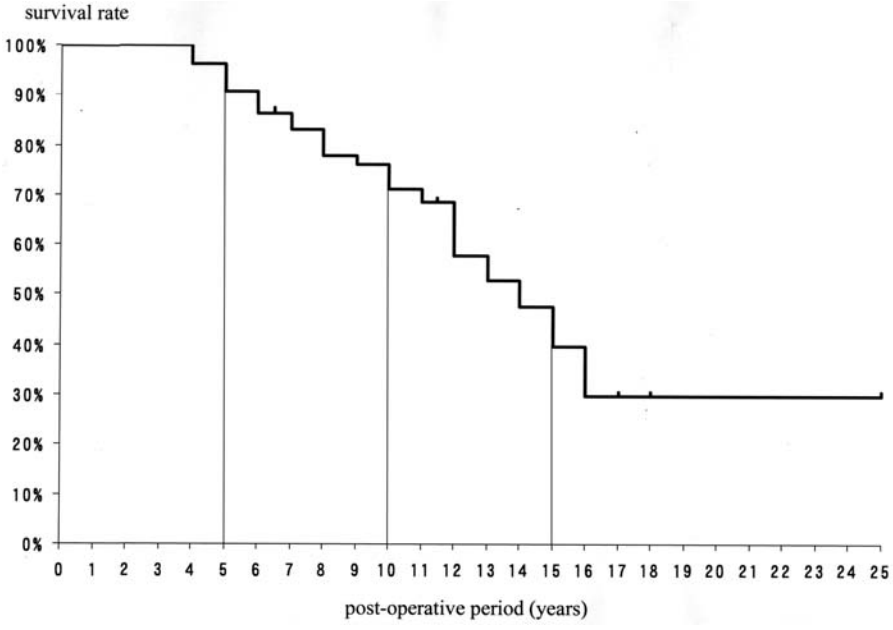

Fig. 8. Vital prognosis: Kaplan-Meier survival curve. The survival rate was 90% in the 5th year after the first surgery, 71% in the 10th year, and 48% in the 15th year. The rate decreased rapidly after more than 10 years after the first surgery

patients who had received old-type implants. It is expected that the number of patients who develop such complications will decrease in the future with advances in the biomaterials used for arthroplasty as well as in the operative techniques.[12] Since it is expected that the vital prognosis will improve and the number of elderly patients will increase, however, continued special attention should be paid to deep infection[13] and fracture.[14] It is important to educate patients[15] about daily living skills, such as good posture for prevention of cervical lesions, prevention of falls, moderate exercise, and continuation of RA treatment, in order to maintain favorable ADL and QOL.

As for the long-term outcome, the vital prognosis was not necessarily good. The survival rates were 90% in the 5th year after the first surgery, 71% in the 10th year, and 41% in the 15th year. The vital prognosis in RA patients is shorter than that in other adults,[16] and many studies have indicated that this trend is more marked in patients who have undergone multiple arthroplasty and in those with arthritis mutilans.[2,17,18] Previous studies[16] on the causes of death in RA patients found that cardiovascular disease, including cerebrovascular accident, was the cause in 43%, malignancy in 13%, infection in 13%, and rheumatic diseases such as vasculitis, rheumatoid lung, and amyloidosis in 6.9%. The current most common causes of death in Japanese adults are cancer, cerebrovascular accident, and cardiac disease, in that order, but the major causes of death in RA patients are infection, typified by pneumonia and organ lesions associated with RA. Caution should be taken against infection, particularly in patients with decreased ADL. In patients with persistent high RA activity, organ lesions associated with RA such as interstitial pneumonia and secondary amyloidosis easily develop. Therefore, drug therapy and appropriate rehabilitation should be performed even in patients who have undergone multiple arthroplasty to prevent generalized RA inflammation. The vital prognosis of patients who have undergone arthroplasty is improving with the spread of knowledge of RA treatment and advances in drug therapy and surgical therapy.[19] Further advances in RA treatment, including biological products and the spread of knowledge regarding the significance of early diagnosis and the early start of treatment of RA will contribute to a decrease in the number of patients with multiple joint destruction. However, patients requiring multiple arthroplasty will still exist, and surgery as a measure to maintain long-term functional and vital prognoses will enhance the value of multiple arthroplasty.

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