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Risk factors affecting the onset of adverse reaction to metal debris after metal-on-metal total hip arthroplasty with a focus on serum metal ion concentrations

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Abstract

Objective: This study was performed to investigate risk factors affecting the onset of adverse reaction to metal debris (ARMD) after metal-on-metal total hip arthroplasty (THA).

Methods: Of the patients who underwent metal-on-metal THA as a primary surgery from January 2007 to August 2011, we included 48 patients in whom the serum metal ion concentrations were measured postoperatively. For these patients, we examined the relationship of the serum cobalt ion concentration with sex, age, Japanese Orthopaedic Association (JOA) hip score as a preoperative clinical evaluation parameter, body mass index (BMI), femoral head diameter, cup abduction angle, height of cup positioning, and magnetic resonance imaging (MRI) findings.

Results: No correlation was observed between the serum cobalt ion concentration and age, sex, preoperative JOA hip score, femoral head diameter, cup abduction angle, height of the cup, or MRI findings. Patients with a BMI of >23 kg/m^2 had significantly higher serum cobalt ion concentrations.

Conclusions: We found that a BMI of >23 kg/m^2 is a risk factor for a high serum cobalt ion concentration. We believe that postoperative periodic measurement of the serum cobalt ion concentration in such patients will help to accurately diagnose ARMD and determine treatment strategies.

Keywords: Metal-on-metal THA, Adverse reaction to metal debris (ARMD), Serum metal ion concentration

Introduction

Total hip arthroplasty (THA) is a surgical procedure that has shown stable clinical performance in providing pain relief and restoring function to damaged hips. In recent years, after the introduction of metal-on-metal THA using metal on the sliding surface, some patients have developed a complication known as adverse reaction to metal debris (ARMD). This reaction is caused by the presence of metal powder or metal ions. Such patients require repeat replacement surgery soon after their initial surgery. The purpose of the present study was to examine various risk factors for the onset of ARMD by focusing on serum metal ion concentrations in patients who underwent metal-on-metal THA.

Methods

Of the patients who underwent metal-on-metal THA as a primary surgery from January 2007 to August 2011, we examined 48 patients (11 male, 37 female) in whom measurement of serum metal ion concentrations was performed postoperatively. The underlying disease was hip osteoarthritis in 43 patients, osteonecrosis of the femoral head in 4 patients, and rheumatoid arthritis in 1 patient. The type of prosthesis used was a pinnacle cup for the cup side in all cases; for the stem, an AML was used in 22 joints, S-ROM in 9 joints, Replica in 8 joints, and SUMMIT in 9 joints. All cups and stems used were manufactured by DePuy Synthes Joint Reconstruction (Warsaw, IN, USA).

For all patients, we examined the relationship of the serum metal ion concentrations with sex, age, Japanese Orthopaedic Association (JOA) hip score as a preoperative clinical evaluation parameter, body mass index (BMI), femoral head diameter, cup abduction angle, height of cup positioning, and magnetic resonance imaging (MRI) findings using the Hauptfleisch classification.[1]

The present study was approved by the Ethical Review Board for Epidemiological and Clinical Research at Fujita Health University (Study of adverse reaction to metal debris after total hip arthroplasty; Approval number: HM14-087). The Mayo Medical Laboratories (Rochester, MN, USA) was commissioned to measure the patients' cobalt ion concentrations using the inductively coupled plasma mass spectrometry method, and the LSI Medience Corporation (Tokyo, Japan) was commissioned to measure the patients' chromium ion concentrations using atomic absorption spectrometry.

According to the Japanese Society for Replacement Arthroplasty guidelines regarding complications of metal-on-metal THA, a careful follow-up is indicated for patients with whole blood and serum cobalt and chromium ion concentrations exceeding 7 ppb (7 μg/L) and 4.5 ppb (4.5 μg/L), respectively. No patients in our department have had a chromium ion concentration exceeding 4.5 ppb; thus, in the present study, we primarily examined the cobalt ion concentration. We used the

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Spearman rank correlation coefficient for the statistical analysis. We used an unpaired t-test to compare the two groups. A p value of ≤0.05 was considered statistically significant.

Results

The patients' baseline characteristics are summarized in Table 1. The mean age of the patients at the time of surgery was 57.1 (range, 31–74) years, and no correlation was observed with the

Table 1 Patients' baseline characteristics

Patient no.	Age (years)	Sex	BMI (kg/m²)	Primary disease	Stem model	Preoperative JOA hip score	Femoral head diameter (mm)	Cup abduction angle (°)	Height of cup positioning (mm)	Serum cobalt ion concentration (μg/L)	MRI findings (Hauptfleisch classification)
1	62	Female	24.3	OA	AML	41	36	45	20	0.3	—
2	56	Female	17.2	OA	AML	38	28	41	28	1.3	—
3	74	Female	22.5	OA	AML	49	36	53	28	1.3	0
4	46	Female	17.5	RA	AML	31	28	35	23	1.4	—
5	61	Female	21.1	OA	AML	33	28	37	24	1.8	—
6	46	Male	21.4	ION	AML	42	28	46	26	3.2	0
7	72	Male	23.0	OA	AML	37	28	41	22	3.7	—
8	66	Male	22.0	OA	AML	32	28	37	17	4.1	—
9	48	Female	25.0	OA	AML	41	28	45	20	5.2	1
10	73	Female	24.1	OA	AML	38	28	42	29	6.0	—
11	61	Male	24.4	OA	AML	34	28	38	17	7.0	—
12	70	Female	21.3	OA	AML	35	28	39	17	8.4	0
13	72	Female	22.6	OA	AML	23	28	27	14	8.7	—
14	58	Female	23.8	OA	AML	44	28	48	17	11.0	1
15	57	Female	24.4	OA	AML	40	28	44	32	13.0	—
16	57	Female	21.2	OA	AML	39	28	43	29	13.0	—
17	54	Female	21.5	OA	AML	33	28	37	24	19.0	1
18	50	Female	23.9	OA	AML	34	28	38	25	20.0	—
19	47	Female	26.0	OA	AML	42	28	46	19	22.0	—
20	58	Female	29.3	OA	AML	36	28	40	27	35.0	0
21	58	Female	25.5	OA	AML	55	28	59	18	44.0	—
22	61	Male	23.5	OA	AML	34	28	38	18	141	2
23	58	Male	24.4	OA	S-ROM	41	36	45	25	0.8	—
24	48	Male	21.3	OA	S-ROM	38	28	41	22	0.8	0
25	47	Male	23.8	OA	S-ROM	29	36	33	25	1.0	—
26	59	Female	27.4	OA	S-ROM	44	28	48	21	1.5	—
27	68	Male	20.6	OA	S-ROM	55	36	59	25	1.6	—
28	50	Female	28.8	OA	S-ROM	44	28	48	23	1.9	—
29	60	Female	26.7	OA	S-ROM	19	28	43	24	2.3	—
30	52	Female	28.5	ION	S-ROM	42	28	46	25	2.7	—
31	68	Male	23.7	ION	S-ROM	36	36	40	23	3.6	—
32	63	Female	27.1	OA	Summit	19	36	40	22	0.3	—
33	60	Female	22.4	OA	Summit	42	28	47	27	0.5	—
34	63	Female	26.3	OA	Summit	51	28	55	18	0.6	—
35	65	Female	23.5	OA	Summit	40	28	44	24	0.6	—
36	50	Female	20.7	OA	Summit	42	28	49	25	0.8	0
37	36	Female	19.5	ION	Summit	44	28	48	24	1.1	—
38	61	Female	26.7	OA	Summit	41	28	45	27	1.1	—
39	58	Female	20.8	OA	Summit	32	28	38	21	1.4	1
40	31	Female	22.4	OA	Summit	40	28	50	27	0.8	—
41	42	Female	16.9	OA	Replica	38	28	54	26	1.1	—
42	52	Male	25.9	OA	Replica	31	36	35	17	3.0	—
43	50	Female	26.1	OA	Replica	43	28	47	20	3.3	—
44	66	Female	23.2	OA	Replica	48	28	53	29	3.3	—
45	54	Female	20.6	OA	Replica	39	28	43	20	6.3	—
46	52	Female	25.8	OA	Replica	39	36	43	24	8.8	—
47	62	Female	24.8	OA	Replica	41	28	45	21	10.0	—
48	52	Female	24.6	OA	Replica	37	28	41	17	11.0	—

OA: osteoarthritis, RA: rheumatoid arthritis, ION: idiopathic osteonecrosis, BMI: body mass index, JOA: Japanese Orthopaedic Association, MRI: magnetic resonance imaging serum cobalt ion concentration (Figure 1). Likewise, no correlation was observed between sex and the serum cobalt ion concentration (Figure 2). The mean preoperative JOA hip score was 38.8 points [standard deviation (SD), 12.1], and no correlation was observed with the serum cobalt ion concentration (Figure 3). The mean BMI was 23.5 kg/m^2 (SD, 2.8), and patients with a BMI of >23 kg/m^2 had significantly higher serum cobalt ion concentrations ($p=0.02$) (Figure 4). The femoral head diameter was 28 mm in 39 patients and 36 mm in 9 patients, but no correlation was observed with the serum cobalt ion concentration (Figure 5). The mean cup abduction angle was 43.7 degrees (SD, 6.5), and seven patients had a steep positioning exceeding 50 degrees. There was no correlation between the abduction angle and serum cobalt ion concentration (Figure 6). The height of the cup was positioned between the teardrop line and the center of the femoral head. The mean height was 22.8 mm (SD, 4.5), with the cup positioned mainly in the true acetabulum. No correlation was observed between the height of the cup and the serum cobalt ion concentration (Figure 7). Postoperative MRI was possible in 38 patients. According to the

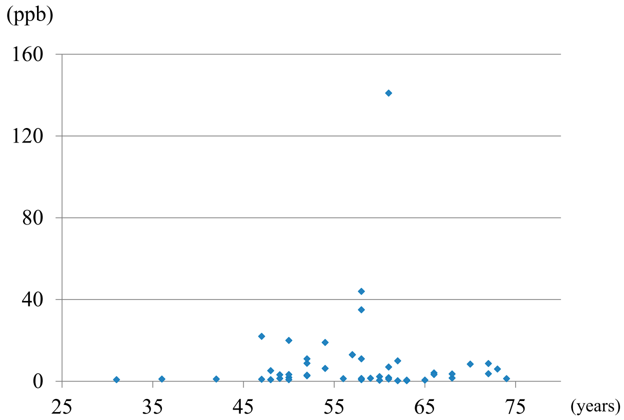

Figure 1 Serum cobalt ion concentration and age of patients at operation
The mean age of the patients at the time of surgery was 57.1 (range, 31–74) years, and no correlation was observed with the serum cobalt ion concentration.

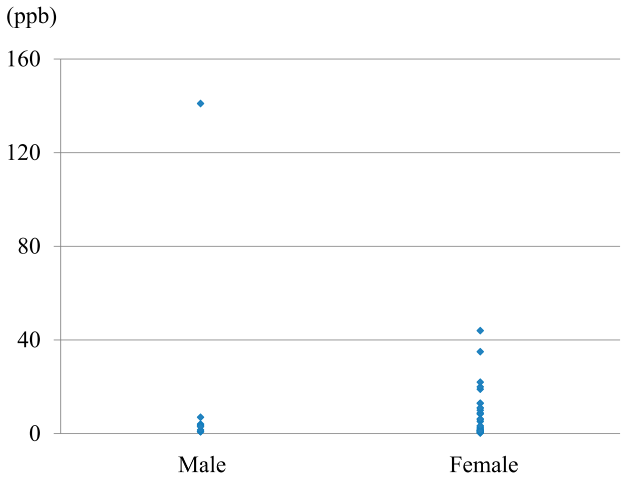

Figure 2 Serum cobalt ion concentration and sex
No correlation was observed between sex and the serum cobalt ion concentration.

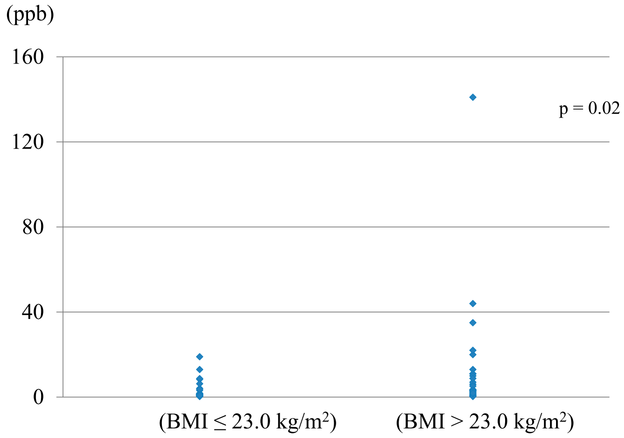

Figure 4 Serum cobalt ion concentration and body mass index (BMI)
The mean BMI was 23.5 kg/m^2 (standard deviation, 2.8), and patients with a BMI of >23 kg/m^2 had significantly higher serum cobalt ion concentrations ($p=0.02$).

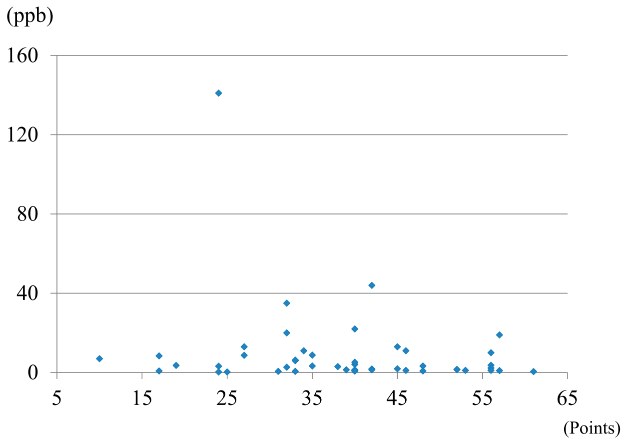

Figure 3 Serum cobalt ion concentration and preoperative Japanese Orthopaedic Association (JOA) hip score
The mean preoperative JOA hip score was 38.8 points (standard deviation, 12.1), and no correlation was observed with the serum cobalt ion concentration.

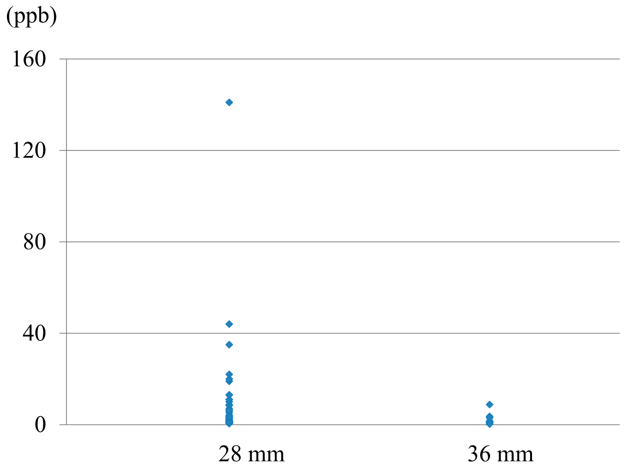

Figure 5 Serum cobalt ion concentration and femoral head diameter
The femoral head diameter was 28 mm in 39 patients and 36 mm in 9 patients, but no correlation was observed with the serum cobalt ion concentration.

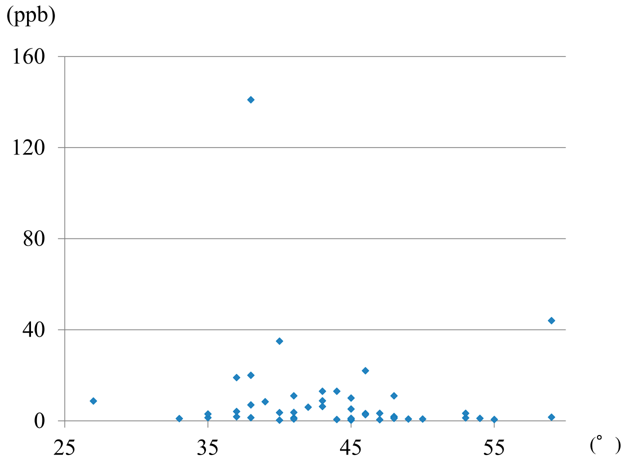

Figure 6 Serum cobalt ion concentration and cup abduction angle
The mean cup abduction angle was 43.7 degrees (standard deviation, 6.5). There was no correlation between the abduction angle and serum cobalt ion concentration.

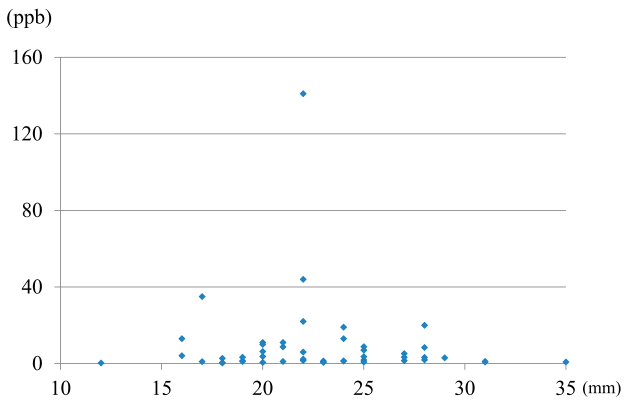

Figure 7 Serum cobalt ion concentration and height of the cup
The mean cup height was 22.8 mm (standard deviation, 4.5). No correlation was observed between the height of the cup and serum cobalt ion concentration.

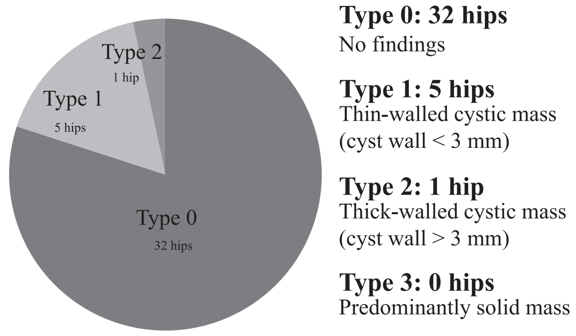

Figure 8 Magnetic resonance imaging (MRI) findings according to the Hauptfleisch classification
Postoperative MRI was possible in 38 patients. According to the Hauptfleisch classification,[1] type 0 (no abnormal findings) was observed in 32 patients, type 1 (thin-walled cystic mass) in 5 patients, type 2 (thick-walled cystic mass) in 1 patient, and type 3 (a predominantly solid mass) in 0 patients.

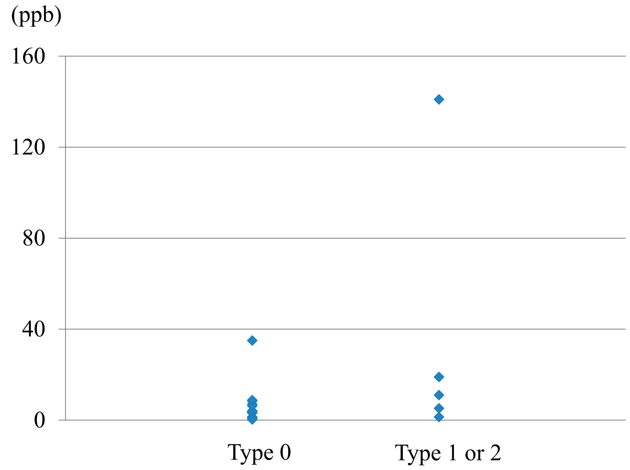

Figure 9 Serum cobalt ion concentration and magnetic resonance imaging (MRI) findings
Serum metal ion concentrations could be measured in 11 patients, in whom type 0 was observed in 6 patients, type 1 in 4 patients, and type 2 in 1 patient. We compared the six patients with type 0 who had no abnormal MRI findings and the five patients with types 1 and 2 who had abnormal MRI findings, but no correlation was observed between the serum cobalt ion concentration and MRI findings.

Hauptfleisch classification,[1] type 0 (no abnormal findings) was observed in 32 patients, type 1 (thin-walled cystic mass) in 5 patients, type 2 (thick-walled cystic mass) in 1 patient, and type 3 (a predominantly solid mass) in 0 patients (Figure 8). Serum metal ion concentrations could be measured in 11 of these patients, among whom type 0 was observed in 6 patients, type 1 in 4 patients, and type 2 in 1 patient. We compared the 6 patients with type 0 who had no abnormal MRI findings and the 5 patients with types 1 and 2 who had abnormal MRI findings, but no correlation was observed between the serum cobalt ion concentration and MRI findings (Figure 9).

Discussion

Sex, age, preoperative JOA hip score, and BMI are patient-related factors that serve as indicators of general activity and can thus be considered as factors that affect mechanical stress applied to THA.

Among patients who undergo metal-on-metal THA, male patients and those with high preoperative JOA hip scores reportedly have significantly higher postoperative metal ion concentrations.[2] Male patients are generally thought to have a higher body weight and higher level of activity than female patients; thus, greater mechanical stress may be applied to the prosthesis. High mechanical stress increases the load on the sliding surface and head–neck junction and is therefore assumed to exacerbate the release of serum metal ions. In our department, we observed no significant difference in metal ion concentrations with respect to sex, age, or preoperative JOA hip scores. However, we found that patients with a BMI of ≥23 kg/m^2 had significantly higher metal ion concentrations. We believe that this is because a greater BMI increases the load on various metal interfaces by which metal ions can be released, such as the head–neck junction and metal sliding surfaces. We were unable to reach a clear conclusion regarding the relationship between the femoral head diameter and metal ion concentrations. Some reports have indicated that a larger femoral head is associated with a higher metal ion concentration.[3,4] The Medicines and Healthcare Products Regulatory Agency (MHRA) of the United Kingdom recommends that patients with a femoral head diameter of ≥36 mm are at high risk and should thus undergo more frequent follow-up observations and metal ion measurements.[5] In particular, the head–neck junction of the prostheses commonly used at our department, including the AML, Replica, and S-ROM from DePuy, have a 9/10 tapered narrow neck. Therefore, in the event of a large femoral head, movement of the femoral head places greater stress on the head–neck junction. This causes corrosion of the head–neck junction, which we believe leads to abundant metallic debris and metal ions. In contrast, some studies have shown that patients with a small femoral head tend to have increased postoperative metal ion concentrations[6] and that there is no relationship between the femoral head size and postoperative metal ion concentrations.[7,8] In the present study, we found no correlation between the femoral head size and ion concentrations. Generally speaking, the degree of obesity of patients undergoing THA in Japan is lower than that in Europe and the United States, and even in patients with a large femoral head, the mechanical stress applied to the head–neck junction is thought to be lower in Japanese than Western patients. Another study showed that in patients with steep cup positioning, the postoperative serum ion concentrations were significantly increased, which could be a risk factor for ARMD.[9] This may be attributed to the fact that a steeper cup position applies greater stress on both the head–neck junction and load-bearing portion of the sliding surface. When the cup abduction angle is optimal in metal-on-metal THA, the wear rate goes through a bedding-in phase followed by a steady-state phase, when fluid lubrication can be achieved, thereby reducing the amount of friction. However, when the cup abduction angle is large, it is thought that fluid lubrication cannot be achieved; this results in edge loading, which increases the amount of friction. It is also thought that the height of the cup placement affects the resultant hip joint force. Generally, it is mechanically ideal to place the cup at the height of the true acetabulum during THA. Higher placement results in greater stress applied to the cup and sliding surface. Abductor muscle weakness might also be associated with increased stress to the cup and sliding surface. In our department, however, only one patient had a cup abduction angle of ≥50 degrees and serum cobalt concentration of >7 ppb, and no significant correlation was observed between the cup abduction angle and serum cobalt concentration. Furthermore, no significant difference was observed in in the serum cobalt concentration with respect to cup height.

Additionally, no significant difference in the serum metal ion concentrations was observed based on the presence or absence of MRI abnormalities. We attribute this to the small number of patients and the fact that false-positive MRI findings were included in type 1. Following THA with a ceramic-on-polyethylene or ceramic-on-ceramic sliding surface, changes in signal intensity are often seen on MRI in the area of the prosthesis. Such changes are simply considered to be postoperative soft tissue changes and involve fluid retention in the synovial bursa. These changes, which are unrelated to ARMD, can be deemed type 1. If more patients had exhibited a Hauptfleisch classification of type 2 or 3, we might have found a significant difference.

Therefore, we observed a significant difference in the postoperative serum metal ion concentrations only with respect to the BMI. As mentioned above, the factors examined in the present study include those thought to possibly affect the sliding surface and head–neck junction. The mean degree of obesity in patients of the present study was indicated by a BMI of 23.4 kg/m^2, which is lower than that of Western patients; thus, the low absolute mechanical stress applied to the sliding surface and head–neck junction of the prosthesis could have resulted in difficulties finding a significant difference.

Many risk factors for increased serum metal ion concentrations have been reported; however, studies of such factors remain inadequate. In particular, these reported risk factors include steep cup placement, highly active patients, obesity, and a high femoral head diameter, all of which are factors that increase the mechanical stress in the sliding surface and head–neck junction. In the present study, we observed a relationship with BMI only; however, we believe that careful follow-up is needed for patients with other factors that could increase the risk of increased metal ion concentrations.

In the medical device alerts by the MHRA in the United Kingdom and The Hip Society in the United States, the measurement of serum metal ion concentrations is recommended as an important test item for ARMD following metal-on-metal THA. However, the measurement of metal ion concentrations is not included in the postoperative treatment algorithm of the Japanese Society for Replacement Arthroplasty for complications of metal-on-metal THA. One reason for this is that the measurement of serum metal ion concentrations is not covered by the national health insurance; therefore, the cost of this test is incurred by the patient. Although the optimal cutoff value has not been established, we believe that regular postoperative measurement of metal ion concentrations in patients with symptoms suggestive of ARMD, patients with abnormal findings on MRI, and patients with risk factors for increased metal ion concentrations would help to accurately diagnose ARMD and determine the patient's treatment plan.

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