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Original Article

The Relationship between Ambulatory Ability before Surgery and the D-dimer Value after Total Hip Arthroplasty: The Evaluation of Ambulatory Ability by the Timed "Up & Go" Test

Kentaro Sasaki[a]*, Masuo Senda[a], Takashi Ishikura[b], Haruyuki Ota[a], Takeshi Mori[a], Hisashi Tsukiyama[a], Masanori Hamada[c], and Naofumi Shiota[d]

[a]*Division of Physical Medicine and Rehabilitation, Okayama University Hospital, Okayama 700-8558, Japan,*
[b]*Department of Rehabilitation Medicine, Shibata Hospital, Okayama 713-8103, Japan,*
[c]*Division of Rehabilitation, Misasa Medical Center, Okayama University Hospital, Misasa, Tottori 682-0192, Japan, and* [d]*Department of Orthopaedic Surgery, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama 700-8558, Japan*

We examined whether ambulatory ability before surgery might influence the post-operative D-dimer level after total hip arthroplasty (THA). One hundred two patients with hip osteoarthritis receiving THA were included in the current study. The patients were all female, and their ages ranged from 45 to 81 (average 65.0 ± 9.3 years). Age, operated side, body mass index (BMI), disease duration before surgery, pre-operative pain evaluated by visual analogue scale (VAS), total cholesterol value, maximal circumference of the lower leg of the operated side, and timed "Up & Go" test (TUG) before surgery, were retrospectively investigated to examine their relationship with D-dimer levels on post-operative day 7. Patients were divided into 2 groups according to the D-dimer value: over 10 μg/ml (Group D), and under (Group N). Patients in group D (N = 52) were older, had a higher BMI, and had less ambulatory ability than patients in group N (N = 50). As age showed a relationship with the D-dimer value on the 7 th day and TUG results, patients in the 2 groups were further subdivided into 50's, 60's, and 70's age brackets. In the 50's bracket, patients in group D had higher BMI than patients in group N, but time for TUG was not significantly different. In the 60's and 70's bracket, patients in group D had less ambulatory ability than patients in group N, but the time for TUG was not directly correlated with the D-dimer value. The results suggest that pre-operative low ambulatory ability in patients with osteoarthritis over 60 years might influence the post-operative D-dimer after THA, indicating the potential risk for post-operative deep venous thrombosis.

Key words: timed "Up & Go" test, D-dimer, total hip arthroplasty

It is well known that deep venous thrombosis (DVT) occurs with high incidence after orthopedic surgery of the lower extremities. The prevalence of DVT after total hip arthroplasty (THA) is 10.0-40.1% as

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*Corresponding author. Phone: +81-86-235-7752; Fax: +81-86-235-7752
E-mail: me6909@hp.okayama-u.ac.jp (K. Sasaki)

determined by venography [1-4]. The prevalence of pulmonary embolism is about 30% for patients with DVT, and about 10% of cases are fatal [5]. In the chronic state, 34% of patients with DVT develop post-thrombotic syndrome with swelling, pain, and ulcer in the lower extremities [6]. To prevent such risks, early diagnosis and appropriate immediate treatment are essential.

As a screening test for DVT, the measurement of the D-dimer level in the serum is reported to be useful. Shiota *et al.* [1] investigated the changes in the D-dimer levels measured by LPIA after THA; those in the DVT-positive group, as diagnosed by venography, were significantly higher on post-operative day 7 than those in the DVT-negative group. Furthermore, they investigated the cut-off value of the D-dimer on post-operative day 7, and showed that 10 μg/ml was the most sensitive and most specific (sensitivity 95.5%, specificity 96.6%) for detecting DVT complications. Other investigators have reported a relationship between the change in the D-dimer and venography findings after THA. Dunn *et al.* [7] showed that the D-dimer values on post-operative days 1 and 6 after THA were higher in patients with DVT. Jorgensen [8] also reported that patients with DVT complications had elevated D-dimer levels on post-operative days 1 and 10 after THA compared with patients without DVT. These results suggest that the D-dimer levels within 10 days after THA might be a useful parameter for predicting DVT.

As treatments for DVT, drug therapy [9, 10] and intermittent pneumatic compression (IPC) stockings [11], as well as exercise therapy, are known to be useful for DVT prophylaxis. Buehler *et al.* [12] reported that progressive weight bearing immediately after THA without cement prevented proximal DVT. Leali and colleagues [13] also showed the efficiency of early full weight-bearing ambulation after non-cemented total joint replacement combined with epidural anesthesia, aspirin and IPC for the prevention of DVT. However, there are few reports that have examined whether improvement in ambulatory ability before surgery could prevent DVT. McNally *et al.* [14] showed that lower leg with postoperative DVT after THA potentially had decreased venous capacitance and venous outflow before THA. They concluded that the major factor in DVT after THA was venous stasis, and that immobility and reduced muscle activity resulted in a poor venous response. The current study focused on ambulatory ability before surgery, and aimed to examine whether limited ambulatory ability before surgery might be associated with an elevated D-dimer value after THA.

Materials and Methods

Patients. The subjects were patients who received THA in the Orthopedic Surgery Department of Okayama University Hospital from 1998 to 2003. They all underwent a physical examination before surgery. The data of 146 patients were reviewed, and subjects who were selected met all of the following criteria: 1) osteoarthritis of the hip (excluding avascular necrosis, collagen disease, infection or trauma), 2) first joint replacement, 3) no complications during or after surgery (dislocation, ruptured aneurysm, arrhythmia requiring treatment, pneumonia or neuropathy), 4) able to walk on admission (with or without a walking aid), and 5) female. As a result, 102 patients were selected (range 45-81 years, average 65.0 ± 9.3) for the study.

Evaluation. We retrospectively investigated 8 preoperative factors including age, operated side, body mass index (BMI), disease duration before surgery (duration), visual analogue scale (VAS), total cholesterol value (T-cho.) in serum, maximal circumference of the lower leg of the operated side (COLL), and the time required for the timed "Up & Go" test [15] (TUG) for ambulatory ability. VAS was measured using a 100 mm transverse straight line. The left side of the line was 0 (no pain), and the right side was 100 (severe or unbearable pain). The patient checked the part of the line corresponding to the degree of pain they experienced. The TUG consisted of standing up from a chair (seat height 45 cm) and walking straight for 3 m, turning, returning to the chair, and sitting down. Subjects performed it as naturally as possible (speed and/or walking device). We measured the performance time in seconds and adopted the fastest of three trials. VAS was measured after TUG.

D-dimer measurement. The D-dimer was measured on post-operative day 7 using a latex photometric immunoassay system (LPIA). Based on the study by Shiota [1], we also retrospectively divided patients into 2 groups according to the D-dimer level on post-operative day 7; patients with values over 10 μg/ml were placed in group D, and those under 10 μg/ml, in group N. D-dimer was not measured before surgery. Patients received no prophylactic agents before surgery. During surgery, a foot-pump system was worn on the non-operated foot and on both feet from post-operative days 1 to 7. Patients were also encouraged to exercise their operated leg without pain after surgery.

Statistical analysis. The operated side between the 2 groups was compared using the mann-whitney U test, and the other 7 factors were compared using the unpaired *t*-test. To examine the relationship between the D-dimer value on post-operative day 7 and other factors, simple regression analysis was used. For all tests, a P value < 0.05 was considered statistically significant.

Results

Comparison between group D and group N (Table 1). After division of the patients into 2 groups based on their day 7 D-dimer values, group D consisted of 52 patients, and group N, 50. In the comparison of factors between the 2 groups, age ($P = 0.0002$), BMI ($P = 0.0024$) and the time required for TUG ($P < 0.0001$) were significantly different. Patients in the group D were older, had higher BMI values, and had lower ambulatory ability than patients in group N. We analyzed the relationship between the D-dimer value and the three significant factors using simple regression analysis. In the results, TUG and BMI were not correlated with the D-dimer value, but age was closely related with the D-dimer value on post-operative day 7 ($r^2 = 0.35$, $P = 0.048$) (Fig. 1). Furthermore, the time required for TUG was affected by age ($r^2 = 0.18$, $P < 0.0001$) (Fig. 2).

Table 1 Subject characteristics in both groups

	Group D (N = 52)	Group N (N = 50)	P Value
Age (years)	68.5 ± 7.7	61.8 ± 9.3	< .001
Operated side (r/l)	25/27	24/26	> .05
BMI (Kg/m²)	24.1 ± 2.9	22.3 ± 2.8	< .01
Duration (yrs)	7.3 ± 6.2	11.5 ± 11.0	> .05
VAS (mm)	58.8 ± 22.1	54.2 ± 25.3	> .05
Total cholesterol (mg/dl)	214.9 ± 38.7	209.7 ± 38.3	> .05
COLL (cm)	32.3 ± 3.3	31.5 ± 3.8	> .05
TUG (sec)	30.1 ± 21.0	15.7 ± 4.4	< .0001

Each value represents the mean ± SD.
BMI, body mass index; COLL, maximal circumference of lower leg; Duration, duration from onset of osteoarthritis to operation; TUG, the timed "Up & Go" test; VAS, visual analogue scale.

Comparison between group D and group N for each age group. It was necessary to remove the factor of age to investigate whether ambulatory ability affected the elevated D-dimer on post-operative day 7 after THA. We subdivided the patients into 50's, 60's and 70's age brackets and compared the factors between groups D and N for each age bracket. We removed patients in the 40's (7 patients) and 80's brackets (1 patient) because of the relatively low number of patients in each group. There were 20 subjects in the 50's age bracket, 37 in the 60's and 38 in the 70's. In the 50's age bracket, the average age in group D (n = 7) was 53.0 ± 1.7 years and in group N (n = 13) was 53.0 ± 2.8 years.

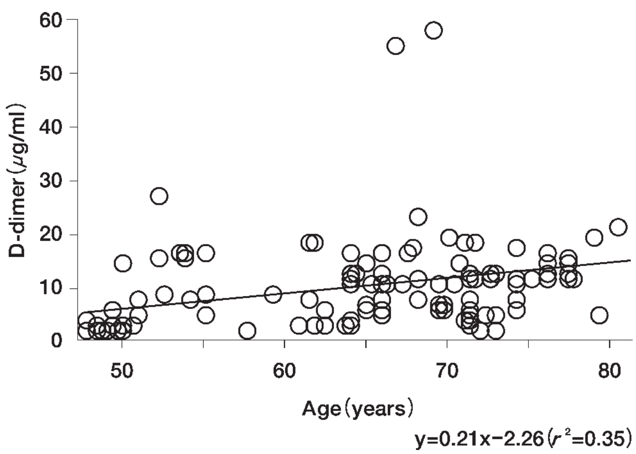

Fig. 1 The correlation between D-dimer value on post-operative day 7 with age of patients.

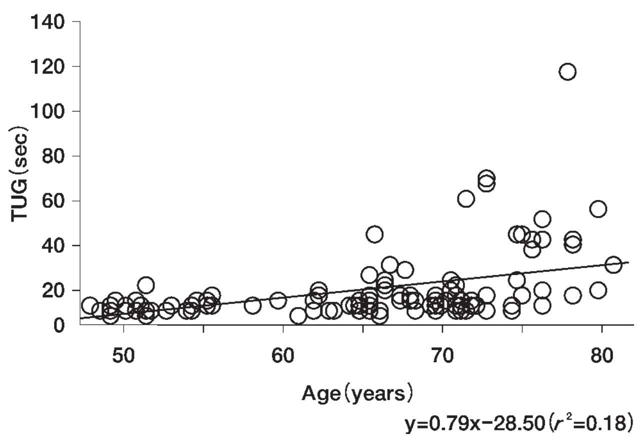

Fig. 2 The correlation between time required for timed "Up & Go" test (TUG) before surgery and the patient's age.

In the 60's, group D (n = 19) was 65.9 ± 2.1 years and group N (n = 18) was 65.3 ± 2.7 years. In the 70's, group D (n = 25) was 74.2 ± 2.8 years and group N (n = 13) was 72.5 ± 2.3 years. Age was not statistically different between groups within age brackets. In the 50's age bracket, only BMI showed a significant difference ($P = 0.0003$). Patients in group D had a higher BMI than patients in group N (Table 2). BMI was also correlated with the D-dimer value on post-operative day 7 ($r^2 = 0.21$, $P = 0.04$) (Fig. 3). In contrast, in the 60's age bracket, only the time of the TUG showed a significant difference between the 2 groups ($P = 0.002$). The patients in group D had lower ambulatory ability than patients in group N (Table 3). Similarly, in the 70's age bracket, patients in group D took more time to perform the TUG ($P = 0.007$) than patients in group N (Table 4); however, the TUG was not correlated with the D-dimer value in simple regression analysis in the 60's and 70's age bracket.

Discussion

We used the timed "Up & Go" test to evaluate ambulatory ability before surgery. The TUG reflects not only the subject's ambulatory ability but also the degree of activity in daily life. Shimada *et al.* [16] investigated the relationship between TUG and activity in daily life. They showed that elderly persons who could finish the TUG (straight distance 5 m) in less than 18 sec had a wide range of activity and used public transport in their daily life. It can be assumed that patients who took more time

Table 2 Subject characteristics in the 50's age bracket in both groups

	Group D (N = 7)	Group N (N = 13)	*P* Value
Age (years)	53.0 ± 1.7	53.0 ± 2.8	> .05
Operated side (r/l)	3/4	9/4	> .05
BMI (Kg/m²)	25.0 ± 1.9	20.7 ± 2.1	< .001
Duration (yrs)	6.9 ± 6.0	12.1 ± 11.6	> .05
VAS (mm)	55.0 ± 13.5	48.5 ± 30.1	> .05
Total cholesterol (mg/dl)	209.7 ± 44.6	216.3 ± 34.3	> .05
COLL (cm)	34.2 ± 1.3	31.8 ± 5.1	> .05
TUG (sec)	17.2 ± 3.7	15.8 ± 3.2	> .05

Each value represents the mean ± SD.

Table 3 Subjects characteristics in the 60's age bracket in both groups

	Group D (N = 19)	Group N (N = 18)	*P* Value
Age (years)	65.9 ± 2.1	65.3 ± 2.7	> .05
Operated side (r/l)	9/10	8/10	> .05
BMI (Kg/m²)	24.3 ± 3.2	23.6 ± 3.1	> .05
Duration (yrs)	9.7 ± 6.3	10.6 ± 10.5	> .05
VAS (mm)	59.2 ± 27.1	57.5 ± 22.2	> .05
Total cholesterol (mg/dl)	225.0 ± 28.1	208.7 ± 40.1	> .05
COLL (cm)	33.2 ± 2.5	31.5 ± 2.3	> .05
TUG (sec)	22.8 ± 9.3	14.8 ± 3.7	< .01

Each value represents the mean ± SD.

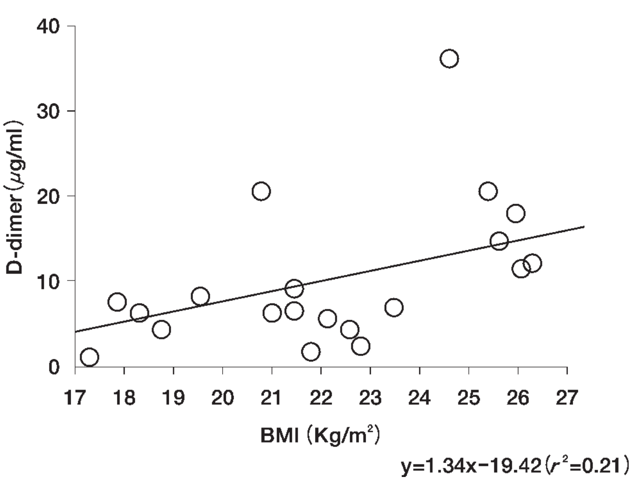

Fig. 3 The correlation between D-dimer value on post-operative day 7 with BMI of patients in the 50's age bracket.

Table 4 Subjects characteristics in the 70's age bracket in both groups

	Group D (N = 25)	Group N (N = 13)	*P* Value
Age (years)	74.2 ± 2.8	72.5 ± 2.3	> .05
Operated side (r/l)	13/12	7/6	> .05
BMI (Kg/m²)	23.6 ± 2.9	22.4 ± 2.5	> .05
Duration (yrs)	5.7 ± 5.7	10.7 ± 12.3	> .05
VAS (mm)	58.4 ± 19.8	45.8 ± 22.8	> .05
Total cholesterol (mg/dl)	210.7 ± 43.4	224.5 ± 31.6	> .05
COLL (cm)	31.2 ± 3.8	31.1 ± 3.0	> .05
TUG (sec)	39.3 ± 26.3	18.1 ± 5.9	< .01

Each value represents the mean ± SD.

for TUG could not move so much in their daily life due to pain, joint dysfunction or muscle weakness. TUG was therefore useful for comprehending in a single measure the individual's activity in pre-operative daily life.

The result of the current retrospective study showed that patients with a D-dimer level over 10 μg/ml in their serum on the 7 th day after THA had lower ambulatory ability before surgery than patients with D-dimer levels under 10 μg/ml, especially in the patients over 60 years old. These results indicate that patients over 60 years of age with low ambulatory ability before surgery might have a risk for DVT complication after THA. However, the time of TUG was not directly correlated with the D-dimer value. Our division of the patients into 2 groups according to postoperative D-dimer levels was based on the study by Shiota *et al.* [1].

There seemed to be 2 major limitations in the current study. D-dimer levels are effective in screening for DVT, but they do not completely reflect the existence of DVT. A D-dimer level over 10 μg/ml does not necessarily indicate the existence of DVT. Actually, only 32 of the 52 patients in group D received anti-coagulation therapy due to the existence of free floating thrombosis for prevention of pulmonary embolism. (Another 20 patients in group D had an adherent thrombosis to the vessel wall, so they were received warfarin.) Furthermore, we investigated the D-dimer level on post-operative day 7 only; D-dimer levels were not measured before surgery. Thus, we could not show how much D-dimer elevated after THA, and how many patients with D-dimer levels over 10 mg/ml before surgery were included in the current study. Therefore, we excluded from this study patients with a past history of DVT, or medication by drugs affecting the coagulation system. There are also no patients with remarkable symptoms of DVT before surgery.

Because age was the strongest factor for the elevation in D-dimer, we subdivided patients into age brackets. As a result, factors influencing the D-dimer level were different between patients over and under 60 years of age. The major reason for this difference could be explained by metabolic change. The basal metabolic rate decreases almost linearly with aging because the volume of skeletal muscle decreases and the percentage of fat tissue increases [17]. According to Shimokata's study [18], the basal oxygen consumption by muscle tissue decreases remarkably from about 60 years of age, although basal oxygen consumption by non-muscle tissue is not influenced. In addition, the waist-thigh ratio or waist-arm ratio reflects the distribution of fat tissue in the body, which begins to increase from about 60 years of age [19]. Thus, the decrease of muscle metabolism is significant in patients over 60 years of age. In patients with arthritis, inactivity-induced muscle atrophy further accelerates the decrease in metabolism with aging, and the decrease of muscular pumping leads to a decline in venous flow.

Furthermore, hormonal changes should be also considered. Our patients were all females, whose estrogen and progesterone secretion may decrease at post-menopause. Estrogen has the function of vasodilation and increasing high-density lipoprotein. The decrease of this hormone is well known to be associated with progressing arterio-sclerosis [20]. Although we could not investigate in detail the relationship between estrogen and D-dimer levels, the hormonal imbalance of the post-menopause phase may also affect the fibrinolysis system in the veins.

Although the number of the patients in the current study was limited, high BMI was a significant factor for the elevation in D-dimer levels after THA in patients under 60 years of age. Ageno *et al.* [21] reported that BMI was significantly correlated with the development of post-thrombotic syndrome, and BMI more than 28 Kg/m^2 was a high risk. Our results showed that total cholesterol was not a significant factor for D-dimer levels over 10 μg/ml, but the increase of fat tissue could influence not only the decrease of muscle metabolism, but also vessel wall or blood viscosity[14].

The basal metabolic rate is also affected by the degree of individual activity, which declines with aging. Ota *et al.* [19] reported that activity in daily life was closely related to the basal metabolic rate of people over 60 years of age; those with high activity levels have a higher basal metabolism than sedentary people. They also showed that aerobic exercise could raise muscle metabolism. Williamson *et al.* [22] also reported the acute effect of resistance exercise in increasing the basal metabolic rate of men over 59 years. However, it is difficult for patients with osteoarthritis to do this exercise effectively. Physical therapy is a known as one of the treatments of osteoarthritis [23-25]. Gilbey *et al.* [23] investigated the effect of a 7-week customized exercise program before THA. The results of their study showed that the exercise group improved hip strength and patients' scores on the Western Ontario and McMaster Universities Osteoarthritis Index (total score, stiffness, and physical function components) before surgery. Thus, we believe exercise therapy before THA can improve impairment or disability for patients with end-stage hip arthritis. The improvement of muscle metabolism might contribute to increasing the blood flow [14], resulting in a lower risk of DVT.

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