ORIGINAL

Early ambulation after total knee arthroplasty prevents patients with osteoarthritis and rheumatoid arthritis from developing postoperative higher levels of D-dimer

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Abstract : This study aimed to clarify the therapeutic effects of postoperative ambulation after total knee arthroplasty (TKA) on deep venous thrombosis (DVT) in patients with osteoarthritis (OA) and rheumatoid arthritis (RA) after TKA. Subjects of this study were thirty-seven inpatients (21 inpatients : OA, 16 inpatients : RA) undergoing TKA (32 female and 5 male). Subjects were divided into two groups, deep venous thrombosis (DVT) group (n=25) and non-DVT group (N group, n=12). The cutoff value was 10.0 μg/ml plasma D-dimer level measured on 7th postoperative day. The N group was below the cutoff value. Another cutoff value divided into two groups, ambulatory group (n=26) and non-ambulatory group (n=11). Ambulatory group was the date of ambulation beginning below 7th day. Statistical analysis confirmed that all subjects showed a significant correlation to the date of ambulation. Postoperative ambulation beginning had strong association with the level of D-dimer (r=0.71). Group comparison showed that the non-ambulatory group had significant higher values of D-dimer than ambulatory group (P=0.022). Typical case supported these results. Postoperative early ambulation within a week after TKA kept patients with OA and RA after TKA lower level of D-dimer. J. Med. Invest. 57 : 146-151, February, 2010

Keywords **:** *DVT, TKA, early ambulation*

INTRODUCTION

The Japanese Guideline for the prevention of venous thromboembolism (1) positions postoperative orthopedic surgery as a high risk for DVT, especially TKA. DVT has been recognized as a common complication for inpatients undergoing TKA (2-4). DVT causes edema and leg pain, and secondary pulmonary embolism (PE), a fatal complication (5, 6). Prophylaxis (7-9) for DVT decreases fatal secondary PE and permits safe postoperative rehabilitation for convalescents. Prophylaxis after TKA consists of anticoagulant therapy, intermittent calf muscle pumping, elastic stockings, continuous passive motion and early getting out of bed as a standardized clinical path in our hospital.

Plasma D-dimer levels increase following orthopedic surgery, including THA, TKA, and open reduction of hip fracture (10, 11). D-dimer assay is a reliable method for ruling out DVT and can be used as a

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routine screening test in the rehabilitation setting (12). Shiota et al. showed a cutoff value of D-dimer 10.0 μg/ml on day 7 in 2002 and the cutoff value was the most sensitive (THA 95.5% ; TKA 94.4%) and most specific (THA, 96.9% ; TKA, 90.0%) in the diagnosis of DVT after THA as well as TKA (13).

Patients with lower activities after TKA had tendencies of higher values of postoperative D-dimer in our hospital. The purpose of this study was to clarify the preventive effects of postoperative physical activities especially in early ambulation on DVT in patients with OA and RA after TKA.

MATERIALS AND METHODS

Subjects

Thirty-seven inpatients undergoing TKA were studied, 32 female and 5 male, in our hospital in 2006-2007. Table 1 shows the preoperative characteristics of inpatients. The mean age at the time of surgery was 72.8 years (range, 63-82 years). The diagnosis included 21 osteoarthritis (OA) and 16 rheumatoid arthritis (RA). All inpatients had postoperatively received warfarin, used a foot-pump system and elastic stocking since 1st day, and undergone continuous passive motion since the 2nd day as DVT prophylaxis.

Table 1. Characteristics of the subjects (N=37)

	Median	25th-75th percentile)
Age (y)	75.0	69.0-78.0
Height (m)	1.5	1.4-1.5
Weight (kg)	59.0	49.0-63.5
BMI (kg/m^2)	26.4	23.1-28.2
Contraction period (y)	10.0	6.0-15.5
Number of underlying diseases	3	2-4
Preoperative D-dimer (μg/ml)	2.1	0.9-5.9
FBS (mg/dl)	111	96-127
VAS (cm)	6.7	6.0-8.0
ADL (score)	38	35-39

Assessments of physical function

Physical assessments gave essential information pre and postoperatively. Basic information consisted of age, sex, body mass index (BMI), fasting blood sugar (FBS), and the number of underlying diseases (high blood pressure, diabetes mellitus, obesity, hyperlipidemia, cardiovascular disease) based on medical records. Preoperative assessments were range of motion (ROM : knee), date of beginning ambulation, activity of daily living score (ADL), activities parallel to the daily living score (APDL), and pain scale (visual analogue scale : VAS). Assesments of ADL and APDL were showed in Table 2. Postoperative assessments were initial date of activities (bedside activities, sitting, standing, ambulation).

Classification of DVT occurrence

The cutoff value of D-dimer, 10.0 μg /ml on day 7 (D-d7) was an indication of DVT (12). D-d7 was measured by the latex agglutination D-dimer measurement on the ACL top automated analyzer for excluding acute deep vein thrombosis, using fibrin degradation products (LPIA FDP-p : FDP-P), which was as a routine laboratory procedure and repeated once a week until 5 weeks during the hospital stay. D-d7 divided patients into 2 groups, positive DVT (DVT group) and non-DVT (N group). The value of D-dimer was over the cutoff value in the DVT group. .

Procedure and Statistical analysis

We performed statistical analyses as follows :
1) Relationships between D-d7 and physical assessment in all patients.

Pearson's correlation analysis and simple regression were used to assess the relationships between D-d7 and physical assessments. Preoperative variable consist of age, sex, BMI, the number of disease complication, abilities of ambulation, ADL and preoperative D-dimer. Postoperative variable consist of

Table 2. Assessments of ADL and APDL scores

ADL	score (1-5)	APDL	score (1-5)
Feeding	1.2.3.4.5	Shopping	1.2.3.4.5
Dressing	1.2.3.4.5	Cooking	1.2.3.4.5
Toilet use	1.2.3.4.5	Cleaning	1.2.3.4.5
Bathing	1.2.3.4.5	Laundry	1.2.3.4.5
Grooming	1.2.3.4.5	Cash management	1.2.3.4.5
Dental health	1.2.3.4.5	Transportation use	1.2.3.4.5
Mobility	1.2.3.4.5	Patient compliance	1.2.3.4.5

Total score ranges 7-35 (1 : dependent, 2 : needs help, 3 : needs watching, 4 : independent with any aids, 5 : independent)

age, sex, BMI, the date of activities beginning such as bedside sitting, standing, wheel chair and toilet (these activities were done on the same day, the date of ambulation).

2) Predictor of postoperative D-d7

Multiple regression analysis was used to determine the associations between D-d7 and physical assessments. We used D-d7 as an outcome variable and pre and postoperative physical assessments as explanatory variables which correlated in procedure 1. Two models of multiple regression analysis were used to assess factors that may explain the variability in the values of D-d7 : 1. The variables entered in model 1 were preoperative assessment : age, BMI, primary disease, VAS, FBS, the number of complication, ambulation and ADL score, preoperative D-dimer value ; 2. The variables entered in model 2 were the date of activity acquisition : bedside sitting, standing, wheel chair, ambulation.

3) The difference in physical assessments between DVT and N groups.

Pre- and postoperative most effective physical assessments on D-dimer in procedure 1 and 2 (ambulation) in these two groups were compared by two-sided unpaired test. We compared A) the date of these groups divided by cutoff value (D-d7> 10 μg/ml). B) We also examined subgroup comparison of D-d7 divided by the date of ambulation beginning on 7th day. Ambulatory group included the inpatients that had begun ambulation within postoperative 7th day and non-ambulatory group was others

All *P*-values less than 0.05 were considered significant. All of these analyses were carried out using Microsoft Excel software (Microsoft Corp, Redmond, WA, USA) add-on ekuseru-toukei 2006 version 1.42 (Social Survey Research Information Co., Ltd).

RESULTS

1) Relationships between D-d7 and physical assessment in all patients.

D-d7 had the strongest positive correlations with the date of ambulation beginning (r=0.71, p< 0.001) in the postoperative assessments in Figure 1. Ambulatory delay was caused by the date of activities acquisition (r=0.523) such as bedside sitting and standing. Other pre- and postoperative assessments had no effects upon D-d7. Other relationships of each assessment were that ; Preoperative : age and D-dimer (r=0.50), sex and primary disease (r= 0.32), BMI and the number of complication (r= 0.44), preoperative D-dimer (r=-0.40). Postoperative : age and primary disease (r=0.41).

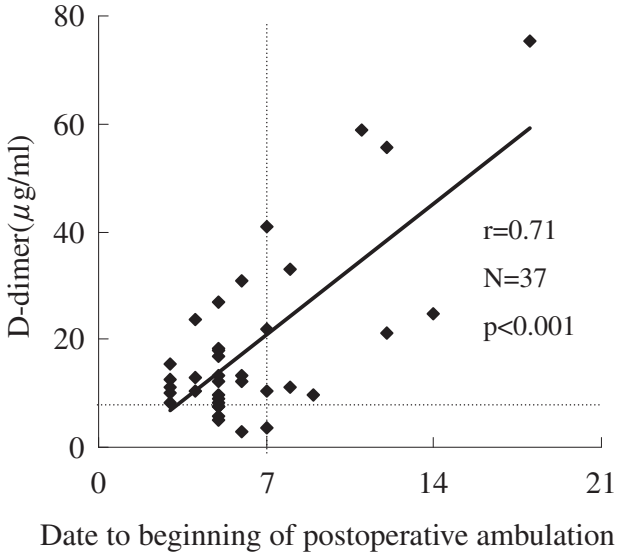

Figure. 1 N=37 (21 OA and 16 RA), the date of ambulation beginning had correlation with the values of D-dimer (r=0.71).

2) Predictor of postoperative D-d7.

Predictors of D-dimer on 7th day were examined by multiple regression analysis in Table 3. The probable determinants of D-d7 were sex (P=0.04), the date of basic activities beginning (P=0.03) and the date of ambulation beginning (P< 0.001) to develop postoperative activities. D-d7 had no probable determinants of preoperative physical assessments.

Table 3. D-d7 and postoperative dependent variable

Activity Acquisition	Parameter Estimate	Standard Error	p-value
Age, y	-0.25	0.21	NS
BMI	-0.59	0.49	NS
Sex	12.24	5.69	< 0.05
Primary disease	-4.01	3.85	NS
Activities beginning	-2.39	1.02	< 0.05
Ambulatory beginning	4.04	0.62	< 0.001

3) The difference in physical assessments between DVT and N groups.

The DVT group included 26 patients and the N did 11 patients with a cutoff value of D-dimer (10.0 μg/ml). A) The date of ambulation beginning did not show significant difference between DVT (mean± SD, 6.77± 3.8 days) and N group (mean± SD, 5.45± 1.5 days) postoperatively by unpaired t test (P= 0.139). The ambulatory group (the date of ambulatory< 7th day) included 25 patients and non-ambulatory (≧7th day) did 12 patients. The D-d7 of non-ambulatory group (mean± SD, 30.5± 22.7 μg/ml) had significant higher difference than ambulatory group (mean± SD, 12.9± 6.7 μg/ml) by unpaired t test (P=0.022).

DISCUSSION

This study shows the significance of postoperative early ambulation following TKA to prevent subsequent DVT and PE. The earlier ambulation began, the lower the 7th day D-dimer level. The D-dimer level following TKA predicts postoperative ambulation for inpatients and other physical functions. Cayley reported that the DVT negative percentage was more than 99.5% when the Wells Scoring System (WSS) was less than score 2 and D-dimer was negative (less than 10 μg/ml) (14). Orthopedic surgery often corresponds to more than score 3 and has a higher risk of DVT in the guidelines. Postoperative D-dimer positive (more than 10 μg/ml) on day 7 was 64.9% (24/37) and D-d7 was 17.0± 14.8 μg/dl in the TKA group (Tokushima University Hospital, 2006-2007). Bed-rest for more than 3 days and clinical signs (lower thigh swelling, leg pain) were DVT risks after TKA in the WSS. The clinical path for TKA in our hospital requires patients to get up within 3 days. The elements of getting out of bed consist of bedside activities, sitting, standing up and ambulation. The results of this study showed that postoperative early ambulation had a significant association with the cutoff value of D-d7.

The American Heart Association lists age more than 60, obesity, and cardiovascular disease as DVT risk factors. This study also could not support other pre- (such as age, sex, primary disease, BMI, FBS, the number of underlying diseases) (2, 15) and postoperative risk factors (such as age, sex, BMI, circumference of calf) (16, 17) except for the date of ambulation and basic activities and sex differences. Female had a significant higher risk for elevation of D-d7, although male was small number in this study. D-d7 was the index of DVT on the 7th day. The non-ambulatory group over a week had significant higher levels of D-dimer than the ambulatory group, implies the importance of early ambulation following TKA within a week. Antigravity activity and weight bearing have been known as common elements for prevention of postoperative D-d7 (DVT) by ambulation promoting calf muscle pumping. Earlier antigravity activities kept D-d7 lower values in this study.

Sasaki reported that the preoperative timed up and go test (TUG) could be suitable to predict D-dimer. The low level of preoperative ambulatory ability was a risk factor of DVT (18). TUG reflected not only the subjects' ambulatory ability but also the degree of activities in daily life. The preoperative ADL score in this study did not have correlation with D-d7. RA showed a higher value of pre and postoperative D-d7 than OA for the primary disease of TKA (15). In this study, average RA was 16.7± 12.1 μg/ml (N=16) and OA was 20.1± 18.7 μg/mil (N=21), which did not show significant difference (P=0.512, Welch's t test). M. McDermott reported that a lower volume of fat and muscle of the triceps lead to higher postoperative D-d7 (16). The preoperative information, based on medical records, appeared suitable for risk management in rehabilitation, we required larger number of subjects.

Postoperative physical assessments include measurement of ROM, circumference, muscle strength and pain. Johanning reported that calf measurement provides an easy and effective means of excluding proximal DVT when screening outpatients. Patients with a circumference of 2.0 cm or less and a negative D-dimer may undergo non-emergent duplex ultrasonography (17).

Early ambulation was often decided by the inpatient's condition or consciousness and was adjusted for each case, which could change the clinical path. The overall first mean day of ambulation was 6.6± 3.7, the earliest was the 3rd day and the latest was the 18th day. Delayed ambulation was often caused by age, patients' intention to rest, postoperative pain, extended use of a wheelchair and short period of self-training. It is important to eliminate these inhibitors of earlier ambulation.

Getting out of bed soon after a procedure is a known postsurgical recommendation. Getting up is an abstract expression and has no definition. Getting up should include not only out of bed but ambulation in this study. Inpatients tend to stay in bed

all the day during hospitalization. Even if they get out of bed, a wheelchair encourages them to stay seated and to move only for rehabilitation exercise. In fact, multiple regression analysis in this study showed that postsurgical ambulation had the strongest effects upon D-d7 than other factors such as age, sex and basic activity beginning. Positive ambulation appears to prevent DVT following TKA and should be encouraged once anticoagulation is instituted, leading to better physical function. The time of beginning ambulation depends on an inpatient's condition or intention. It is necessary to educate inpatients' about earlier postoperative ambulation and obtain preoperative informed consent for a postoperative rehabilitation program.

We had a small number and no control over the data and need to verify the more patients in the future study.

CONCLUSION

Postoperative early ambulation within a week kept patients with OA and RA after TKA lower level of D-dimer.

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