



Is Taking an Antiplatelet Agent a Contraindication for Early Surgery in Displaced Femur Neck Fracture?

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Purpose: The purpose of this study was to evaluate whether we have to stop the antiplatelet agents prior to hemiarthroplasty surgery in patients with displaced femur neck fractures to reduce postoperative complications.

Materials and Methods: We enrolled forty-three patients with displaced femur neck fractures who were treated by bipolar hemiarthroplasty and were taking antiplatelet agents. Group I included 21 patients who discontinued antiplatelet agents and had delayed operations at an average 5.7 days and group II included 22 patients who had early operations within 24 hours without stopping the antiplatelet agents. We compared the pre- and postoperative levels of hemoglobin, the volume of postoperative transfusion requirement and complications. Student's *t*-test and chi-square test were used for statistical analysis.

Results: The average differences between preoperative and postoperative hemoglobin was 1.4 ± 0.4 g/dL decrease in group I and 2.1 ± 0.5 g/dL decrease in group II ($P < 0.001$). Patients who received a blood transfusion were 11 in group I and 13 in group II ($P = 0.66$). Total number of blood transfusion was 13 pints in group I and 18 pints in group II ($P = 0.23$). Pneumonia occurred in one patient in each group. Four pressure sores and three diaper rashes were developed in group I. But there were no patients requiring massive transfusion, reoperation due to hematoma and infection in each group.

Conclusion: Although continuous taking of antiplatelet agents in displaced femur neck fracture is associated with an increased risk of postoperative bleeding, taking an antiplatelet agent itself is not a contraindication of early surgery.

Key Words: Displaced femur, Neck fracture, Antiplatelet agent, Early surgery, Hemiarthroplasty

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INTRODUCTION

Recently, femur neck fractures are increasing in incidence due to the increase of elderly population^{1,2}. Displaced femur neck fractures require an operative treatment. In most of older patients, displaced femur neck fractures were accompanied by complications such as cardiovascular or cerebrovascular diseases, respiratory diseases, which, as a result, caused their high mortality rate and morbidity rate³. There is a controversy about the operative timing for these

patients^{4,5}). It is known that an early operation can reduce the incidence of some complications such as pneumonia, decubitus ulcer, deep vein thrombosis (DVT) and pulmonary thromboembolism caused by the prolonged bed immobilization^{6,7}). Recently, considerable numbers of older patients are taking antiplatelet agents to treat or prevent cardiovascular or cerebrovascular diseases⁸⁻¹⁰). Unfortunately, however, operation of these older patients in most cases should be delayed for the risk of excessive bleeding and prohibition of spinal anesthesia^{11,12}). We divided the patients with displaced femur neck fractures who were taking antiplatelet agents into two groups: those who had a delayed operation after the withdrawal of antiplatelet agents and those who had a relatively early operation within 24 hours without the withdrawal of antiplatelet agents. We intended to compare the changes of the hemoglobin level, transfusion requirement and complications between these two groups.

MATERIALS AND METHODS

We selected 43 patients among those with displaced femur neck fractures caused by low-energy trauma such as trivial from a fall who were taking antiplatelet agents and were treated by bipolar hemiarthroplasty within the period between May 2009 and April 2012 were

retrospectively analyzed by using medical records. We excluded patients who received a preoperative or intraoperative transfusion or had other combined extremity fracture (distal radius or proximal humerus fracture), extraarticular fracture, minimal displaced fracture, pathologic fracture, periprosthetic fracture, coagulopathy and lesser than 60 years old. All of them were taking antiplatelet agents such as clopidogrel (Plavix[®]; Bristol-Myers Squibb, New York, NY, USA), triflusal (Disgren; Myungin, Seoul, Korea), cilostazol (Pletal[®]; Otsuka, Tokyo, Japan) for the prevention and treatment of cardiovascular or cerebrovascular diseases. We explained advantages and disadvantages of the early operation as well as delayed operation to patient and their family members and got their informed consent before the performance of the operation. We divided the group based on the decision and consent given by the patients and their family. Group I patients got a delayed operation with an average of 5.7 days (5-8 days) after the withdrawal of antiplatelet agents and group II patients received an early operation within 24 hours after hospitalization without the withdrawal of antiplatelet agent. We checked the physical status of patients in accordance with American Society of Anesthesiologists Classification¹³). As a result, we found that group I included 11 patients with class 2 and 10 patient class 3, and group II included 10 patients with

Table 1. Basic Preoperative Characteristics of the Patients

Characteristic	Group I	Group II	P-value
Age (yr)	72.9±6.5	73.1±7.7	0.93
Sex (male:female)	5:16	8:14	0.38
ASA grade			
ASA 2	11	10	0.86
ASA 3	10	12	0.65
Comorbidity			
Cerebrovascular disease	12	15	0.46
Hypertension	12	19	0.08
Diabetes mellitus	12	10	0.45
Cardiovascular disease	7	7	0.91
Respiratory disease	4	5	0.53
Renal disease	4	7	0.34
Cognitive disease	1	2	0.32
Cancer	1	0	0.97
Antiplatelet agent			
1	17	16	0.53
2	4	6	0.34

Values are presented as mean±standard deviation or number only.

Group I: included 21 patients who discontinued antiplatelet agents and had delayed operations, group II: included 22 patients who had had early operations, ASA: American Society of Anesthesiologists.

class 2, 12 patients with class 3. There were 5 males and 16 females in group I whose average age was 72.9 ± 6.5 years old (65-91 years). Group II included 8 males and 14 females whose average age of 73.1 ± 7.7 years old (62-88 years). Patients taking one antiplatelet agent were 17 in group I and 16 in group II. Patients taking two antiplatelet agents were 4 in group I and 6 in group II. There were no statistical differences in the aspect of demographic data including comorbidities between these two groups (Table 1).

Seven patients underwent surgery under general anesthesia and 14 patients underwent surgery under spinal anesthesia in group I. All 22 patients in group II got surgery under general anesthesia. All operations were performed by a single experienced surgeon by using the posterolateral approach on the lateral position. Cemented stem (MS-30; Zimmer, Winterthur, Switzerland) was used for 8 patients in both groups and cementless stem (Zimmer) was used for 13 patients in group I and 14 patients in group II, depending on the proximal femoral morphology. Data related to the surgery is shown in Table 2.

We checked the level of preoperative and postoperative hemoglobin level, postoperative transfusion volume and complications between two groups. The preoperative hemoglobin level was based on the value checked one day before surgery in group I and first at the emergency room in group II and the postoperative one was based on the value checked 24 hours after the operation.

Postoperatively, we used intermittent pneumatic compression device for the prevention of DVT but didn't used any kinds of chemical prophylactic agents, also encouraged active mobilization of lower extremities and walking if the pain is tolerable.

The Student's *t*-test and chi-square test were used for

statistical analysis using SPSS program ver 21 (SPSS Inc., Chicago, IL, USA).

RESULTS

Clinical outcomes were summarized in Table 3. Mean value of preoperative hemoglobin was 11.5 ± 1.0 , 11.6 ± 1.1 g/dL in the group I and II ($P=0.60$). The mean value of postoperative hemoglobin was 10.0 ± 1.0 g/dL in group I, 9.6 ± 1.0 g/dL in group II ($P=0.09$). Postoperative decrement of hemoglobin level was 1.4 ± 0.4 g/dL in group I, 2.1 ± 0.5 g/dL in group II ($P<0.0001$). In other words it was confirmed that early operation for the patient who was taking an antiplatelet agent was related with statistically significant postoperative blood loss. However, patients who received a blood transfusion were 11 in group I and 13 in group II ($P=0.66$). Total number of blood transfusion was 13 pints in group I and 18 pints in group II ($P=0.23$) and average transfusion volume per patient was 1.2 pints in group I and 1.4 pints in group II. There was no statistical significant in the number of transfused patients and number of transfused blood bag.

We also performed subgroup analysis. In cemented stem group, mean value of preoperative hemoglobin was 11.0 ± 0.8 , 11.3 ± 1.4 g/dL in the group I and II ($P=0.58$). The mean value of postoperative hemoglobin was 9.6 ± 0.7 g/dL in group I, 9.3 ± 1.1 g/dL in group II ($P=0.62$). Postoperative decrement of hemoglobin level was 1.4 ± 0.2 g/dL in group I, 2.0 ± 0.5 g/dL in group II ($P=0.02$). In cementless group, mean value of preoperative hemoglobin was 11.8 ± 0.9 , 11.9 ± 0.9 g/dL in the group I and II ($P=0.88$). The mean value of postoperative hemoglobin was 10.3 ± 1.0 g/dL in group I, 9.7 ± 0.9 g/dL in group II ($P=0.07$). Postoperative decrement of

Table 2. Data Related Surgery

Parameter	Group I	Group II	P-value
Type of anesthesia			
General	7	22	
Spinal	14	0	
Type of stem			
Cemented	8	8	0.67
Non-cemented	13	14	0.90
Time to surgery from hospitalization (mean)	5.7 days	≤24 hours	
Operation time (minutes)	60.2 ± 11.3	57.3 ± 9.2	0.35

Values are presented as number only or mean ± standard deviation.

Group I: included 21 patients who discontinued antiplatelet agents and had delayed operations, group II: included 22 patients who had had early operations.

Table 3. Clinical Outcomes

Outcome	Group I	Group II	P-value
Preoperative Hb (A) (g/dL)	11.5±1.0	11.6±1.1	0.60
Postoperative Hb (B) (g/dL)	10.0±1.0	9.6±1.0	0.09
Difference between A and B (g/dL)	1.4±0.4	2.1±0.5	<0.0001
Transfusion			
Patient	11	13	0.66
Blood bag (pint)	13	18	0.23
Subgroup analysis			
Cemented stem			
Preoperative Hb (C) (g/dL)	11.0±0.8	11.3±1.4	0.58
Postoperative Hb (D) (g/dL)	9.6±0.7	9.3±1.1	0.62
Difference between C and D (g/dL)	1.4±0.2	2.0±0.5	0.02
Cementless stem			
Preoperative Hb (E) (g/dL)	11.8±0.9	11.9±0.9	0.88
Postoperative Hb (F) (g/dL)	10.3±1.0	9.7±0.9	0.07
Difference between E and F	1.4±0.5	2.0±0.5	0.003
Complication			
Pneumonia	1	1	0.97
Pressure sore	4	0	0.04
Diaper rash	3	0	0.08

Values are presented as mean±standard deviation or number only.

Group I: included 21 patients who discontinued antiplatelet agents and had delayed operations, group II: included 22 patients who had had early operations, Hb: hemoglobin.

hemoglobin level was 1.4±0.5 g/dL in group I, 2.0±0.5 g/dL in group II ($P=0.003$). In both cemented and cementless stem group analysis, early surgery was also related statistically significant postoperative blood loss.

Pneumonia occurred in one patient in each group, but all 2 patients were treated successfully with parenteral antibiotics. Minor complications such as pressure sore and diaper rash related with delayed surgery and preoperative immobilization was more frequent in group I who underwent late surgery. We found no excessive blood loss requiring massive transfusion, formation of hematoma requiring revision surgery, infection associated with hematoma in both groups.

DISCUSSION

As the elderly population is increasing gradually all over the world, it is estimated that 7 million patients with hip fracture will occur in a year in 2050^{2,14,15}. Most elderly patients with hip fracture also suffered more than one underlying medical disease, and their mortality within 1 year after the hip fracture was about 14-37.1%^{8,16-18}. Shiga et al.¹⁷ stated that the mortality rate at 1 month and 12 months of patients having the operation more than 48 hours after the fracture increased 41% and

32%, respectively, compared to those having the early operation within 48 hours after the fracture accident. Moreover, Orosz et al.⁷ said that the early operation decreased the mortality rate, pneumonia, bedsores. In addition, lots of authors recommended early operation if the physical status of patients were optimized for the operation because the delayed operation increased the mortality and morbidity of elderly patients with hip fracture^{6,17,19-21}. However, one of the factors that delay the operation for these patients is antiplatelet agents. When these elderly patients are taking antiplatelet agents, there are many cases in which the operation is delayed because there is a risk of excessive bleeding and prohibition for spinal anesthesia^{11,12}. By now, there has not been a consensus on the proper timing of operation for the elderly patients with hip fractures who are taking antiplatelet agents^{4,5}.

There are antiplatelet agents that elderly patients are taking as follows: clopidogrel, cilostazol, triflusal. Since US Food and Drug Administration approved clopidogrel as an antiplatelet agent in 1997, it has been in use for the prevention and treatment of ischemic stroke, myocardial infarction, or acute coronary artery syndrome^{8-10,22}. It is known that its half-life is 8 hours, and the function of platelet is recovered 5 to 7 days later when new platelet will be generated²³. Cilostazol and triflusal have also

similar antiaggregant effect on platelet. Thus, it is recommended to stop taking these agents for about 5 days before the surgery²⁴⁾.

When performing the early operation for elderly patients with hip fracture who are taking antiplatelet agents, there may be complications arising out of the increase of bleeding and transfusion. On the other hand, when having the delayed operation 5 to 10 days later after the withdrawal of antiplatelet agents, there may be also complications caused by the prolonged bed rest²⁵⁻²⁷⁾. According to Chechik et al.²⁸⁾ they compared the results of the early operation without the withdrawal of clopidogrel with those of the delayed operation performed 5 days later after the withdrawal of clopidogrel. There was no significant difference between these two operations except that the period of hospitalization is longer in the delayed operation than in the early operation. Johansen et al.²⁶⁾ reported that there were a significant increase of complications such as DVT and pulmonary thromboembolism when performing a delayed operation 7.3 days later on average after the withdrawal of clopidogrel. As the delayed operation caused the increase of complications, many authors²⁶⁻²⁹⁾ recommended the early operation even for elderly patients who are taking antiplatelet agents. They also argued that the possibility of complications such as the formation of a hematoma related to bleeding, infection, excessive bleeding, or high mortality rate which arose out of the early operation for the elderly patients who were taking antiplatelet agents was rather relatively smaller than those of the delayed operation until the function of platelet would be recovered^{4,5,26-29)}.

We are making efforts to perform an early operation within 24 hours after the hip fracture, even for patients who are taking antiplatelet agents. Before the operation, we made efforts to identify the overall medical status of patients and to correct any correctable abnormality. For the medical status that cannot be corrected, we had a consultation with the anesthesiologist and then gave the explanation to the patients sufficiently before the operation. An experienced surgeon performed the bipolar hemiarthroplasty, which made it possible to reduce the duration time of operation, intraoperative blood loss and potential chance of infection.

We found that early operation for the patient who took an antiplatelet agent was related with statistically significant postoperative blood loss regardless of selected stem type. The effect of anesthesia like spinal anesthesia can decrease the intra operative bleeding in

group I (14 out of 21) and more number of hypertensive patients in group II (19 out of 22) can be reason for more blood loss in this group. But there was no need of revision surgery in early surgery group, of massive transfusion related postoperative bleeding. On the contrary, minor complications such as pressure sore and diaper rash related with delayed surgery and preoperative immobilization was more frequent in group I underwent late surgery. There was no patient who died within postoperative 3 months.

CONCLUSION

Although continuous taking of antiplatelet agents in displaced femur neck fracture is associated with an increased risk of postoperative bleeding, but taking an antiplatelet agent itself is not a contraindication of early surgery.

The limitation of this study was that it used small number of patients and was based on the results of operations by a single surgeon in one medical center. We think that these limitations can be covered by future research over multicenter study.

REFERENCES

- Gullberg B, Johnell O, Kanis JA. *World-wide projections for hip fracture. Osteoporos Int.* 1997;7:407-13.
- Parker M, Johansen A. *Hip fracture. BMJ.* 2006;333:27-30.
- Roche JJ, Wenn RT, Sahota O, Moran CG. *Effect of comorbidities and postoperative complications on mortality after hip fracture in elderly people: prospective observational cohort study. BMJ.* 2005;331:1374.
- Inman DS, Michla Y, Partington PF. *Perioperative management of trauma patients admitted on clopidogrel (Plavix). A survey of orthopaedic departments across the United Kingdom. Injury.* 2007;38:625-30.
- Lavelle WF, Demers Lavelle EA, Uhl R. *Operative delay for orthopedic patients on clopidogrel (plavix): a complete lack of consensus. J Trauma.* 2008;64:996-1000.
- Al-Ani AN, Samuelsson B, Tidermark J, et al. *Early operation on patients with a hip fracture improved the ability to return to independent living. A prospective study of 850 patients. J Bone Joint Surg Am.* 2008;90:1436-42.
- Orosz GM, Magaziner J, Hannan EL, et al. *Association of timing of surgery for hip fracture and patient outcomes. JAMA.* 2004;291:1738-43.
- Maheshwari R, Acharya M, Monda M, Pandey R. *Factors influencing mortality in patients on antiplatelet agents presenting with proximal femoral fractures. J Orthop Surg (Hong Kong).* 2011;19:314-6.
- CAPRIE Steering Committee. *A randomised, blinded, trial*

- of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). *Lancet*. 1996;348:1329-39.
10. Yusuf S, Zhao F, Mehta SR, Chrolavicius S, Tognoni G, Fox KK; Clopidogrel in Unstable Angina to Prevent Recurrent Events Trial Investigators. *Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation*. *N Engl J Med*. 2001;345:494-502.
 11. Llaur JV, De Andrés J, Gomar C, Gómez-Luque A, Hidalgo F, Torres LM. *Anticlotting drugs and regional anaesthetic and analgesic techniques: comparative update of the safety recommendations*. *Eur J Anaesthesiol*. 2007;24:387-98.
 12. Horlocker TT, Wedel DJ, Benzon H, et al. *Regional anesthesia in the anticoagulated patient: defining the risks (the second ASRA Consensus Conference on Neuraxial Anesthesia and Anticoagulation)*. *Reg Anesth Pain Med*. 2003;28:172-97.
 13. American Society of Anesthesiologists. *New classification of physical status*. *Anesthesiology*. 1963;24:111.
 14. Johnell O, Kanis JA. *An estimate of the worldwide prevalence, mortality and disability associated with hip fracture*. *Osteoporos Int*. 2004;15:897-902.
 15. Morris AH, Zuckerman JD; AAOS Council of Health Policy and Practice, USA; American Academy of Orthopaedic Surgeons. *National Consensus Conference on improving the continuum of care for patients with hip fracture*. *J Bone Joint Surg Am*. 2002;84:670-4.
 16. McLaughlin MA, Orosz GM, Magaziner J, et al. *Preoperative status and risk of complications in patients with hip fracture*. *J Gen Intern Med*. 2006;21:219-25.
 17. Shiga T, Wajima Z, Ohe Y. *Is operative delay associated with increased mortality of hip fracture patients? Systematic review, meta-analysis, and meta-regression*. *Can J Anaesth*. 2008;55:146-54.
 18. Parker MJ, Anand JK. *What is the true mortality of hip fractures?* *Public Health*. 1991;105:443-6.
 19. Hamlet WP, Lieberman JR, Freedman EL, Dorey FJ, Fletcher A, Johnson EE. *Influence of health status and the timing of surgery on mortality in hip fracture patients*. *Am J Orthop (Belle Mead NJ)*. 1997;26:621-7.
 20. Villar RN, Allen SM, Barnes SJ. *Hip fractures in healthy patients: operative delay versus prognosis*. *Br Med J (Clin Res Ed)*. 1986;293:1203-4.
 21. Bredahl C, Nyholm B, Hindsholm KB, Mortensen JS, Olesen AS. *Mortality after hip fracture: results of operation within 12 h of admission*. *Injury*. 1992;23:83-6.
 22. Eisenstein EL, Anstrom KJ, Kong DF, et al. *Clopidogrel use and long-term clinical outcomes after drug-eluting stent implantation*. *JAMA*. 2007;297:159-68.
 23. Weber AA, Braun M, Hohlfeld T, Schwippert B, Tschöpe D, Schrör K. *Recovery of platelet function after discontinuation of clopidogrel treatment in healthy volunteers*. *Br J Clin Pharmacol*. 2001;52:333-6.
 24. Llaur JV, Lopez-Forte C, Sapena L, Ferrandis R. *Perioperative management of antiplatelet agents in noncardiac surgery*. *Eur J Anaesthesiol*. 2009;26:181-7.
 25. Haidar R, Taher AT. *How long should we delay hip fracture surgery for elderly patients on clopidogrel?* *Injury*. 2011;42:1509-10.
 26. Johansen A, White J, Turk A. *Clopidogrel therapy: implications for hip fracture surgery*. *Injury*. 2008;39:1188-90.
 27. Harty JA, McKenna P, Moloney D, D'Souza L, Masterson E. *Anti-platelet agents and surgical delay in elderly patients with hip fractures*. *J Orthop Surg (Hong Kong)*. 2007;15:270-2.
 28. Chechik O, Amar E, Khashan M, Kadar A, Rosenblatt Y, Maman E. *In support of early surgery for hip fractures sustained by elderly patients taking clopidogrel: a retrospective study*. *Drugs Aging*. 2012;29:63-8.
 29. Collinge CA, Kelly KC, Little B, Weaver T, Schuster RD. *The effects of clopidogrel (Plavix) and other oral anticoagulants on early hip fracture surgery*. *J Orthop Trauma*. 2012;26:568-73.