

# Effect of Preoperative Aspirin Use on Postoperative Bleeding and Perioperative Myocardial Infarction in Patients Undergoing Coronary Artery Bypass Surgery

Mohammad Hassan Ghaffarinejad MD, Amir Farjam Fazelifar MD,\*  
Shahram Mohajer Shirvani MD,\* Esmaeel Asdaghpour MD,  
Farzad Fazeli MD and Freidoun Noohi MD\*

## Abstract

**Background-** Continuation or discontinuation of aspirin use in the preoperative period for patients scheduled for elective cardiac surgery has continued to be controversial. In this study, we tried to evaluate clinical outcomes (mortality, postoperative bleeding and perioperative myocardial infarction) in patients who underwent first elective coronary artery bypass grafting and received aspirin during the preoperative period.

**Methods-** The study was a prospective, randomized and single-blinded clinical trial. Two-hundred patients were included in the study and divided into two groups. One group received aspirin 80-160 mg and in the other group, aspirin was stopped at least for seven days before operation. The primary end points of the study were in-hospital mortality rate and hemorrhage-related complications (postoperative blood loss in the intensive care unit, reexploration for bleeding and red blood cell and non-red blood cell transfusion requirements). The secondary end point was perioperative myocardial infarction.

**Results-** There were no differences in patients' characteristics among aspirin users and non-aspirin users. We found a significant difference between postoperative blood loss ( $608 \pm 359.7$  ml vs.  $483 \pm 251.5$  ml;  $P=0.005$ ) and red blood cell product requirements ( $1.32 \pm 0.97$  units packed cells vs.  $0.94 \pm 1.02$  units packed cells;  $P=0.008$ ) in the two groups. There was no significant difference between the two groups regarding platelet requirements and the rate of in-hospital mortality and reexploration for bleeding. Similarly, we found no significant difference in the incidence of definite and probable perioperative myocardial infarction ( $P=0.24$  and  $P=0.56$ , respectively) and in-hospital mortality between the two groups.

**Conclusion-** Preoperative aspirin administration increased postoperative bleeding and red blood cell requirements with no effect on mortality, reexploration rate and perioperative myocardial infarction (*Iranian Heart Journal 2008; 9 (2):18-22*).

**Key words:** aspirin ■ postoperative bleeding ■ perioperative myocardial infarction

**W**e designed a prospective, randomized and single-blinded study for evaluation of preoperative aspirin use on in-hospital mortality, postoperative bleeding and perioperative myocardial infarction.

We found that preoperative aspirin use increases postoperative bleeding, red blood cell and fresh frozen plasma requirements, without a beneficial effect on perioperative myocardial infarction.

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From the Department of Cardiovascular Surgery and \*Cardiology, Shaheed Rajaie Cardiovascular Medical Center, Iran University of Medical Sciences, Tehran, Iran.  
Address for correspondence: Mohammad Hassan Ghaffarinejad, MD, Dept. of Cardiovascular Surgery, Shaheed Rajaie Cardiovascular Medical Center, Iran University of Medical Sciences, Mellat Park, Vali-E-Asr Avenue, Tehran, 1996911151, P.O.Box:15745-1341, Iran.  
Tel: 0098 21 23922931 Fax: 009821-88784618 Email: gafer@rhc.ac.ir

Aspirin is an effective therapy in the management of stable and unstable coronary artery diseases.<sup>1</sup> Early initiation of aspirin after coronary artery bypass graft (CABG) surgery reduces risk of graft occlusion.<sup>2</sup> Aspirin has been implicated in platelet dysfunction and prolongation of bleeding time but its effect on postoperative bleeding, reexploration and blood products requirements is controversial.<sup>3-12</sup> In this study we tried to determine effect of preoperative aspirin use on in-hospital mortality, postoperative bleeding, blood transfusion requirements and perioperative myocardial infarction (MI).

### Methods

We conducted a prospective study on two-hundred patients (67 male aspirin users vs. 70 male non-aspirin users,  $P=0.761$ , mean age  $56.9\pm 9.14$  years in aspirin users vs.  $56.9\pm 9.59$  years in non-aspirin users,  $P=0.83$ ), who underwent CABG surgery in our department between November 2003 and December 2004. We received ethical approval for the study and the patients were enrolled in the study with informed written consent. We included patients who underwent elective CABG for the first time. Our exclusion criteria were: 1) need for concomitant valvular, aortic or aneurysmectomy surgery, 2) concomitant antiplatelet drug consumption (clopidogrel, ticlopidine, glucocorticoids, non-steroidal anti-inflammatory drugs, etc). We routinely used the left internal mammary artery as a conduit, total grafts were less than five and all operations were done by one surgical team. The patients' characteristics are summarized in Table I.

The patients were randomly assigned into one of the two groups: group 1 received aspirin preoperatively and in group 2, aspirin was stopped at least seven days before CABG. All patients received a single dose of aprotinin (2,000,000 units kallikrein inhibitor) once during surgery. Aspirin was started post-

operatively within 6 hours after CABG in the two groups.

**Table I. Patients' characteristics**

Variable	Aspirin group	Non aspirin group	P-value
LV ejection Fraction	41.7±11.6	42.6±11.3	0.69
Cigarette smoking			
Yes	36	36	1.0
No	64	64	
Dyslipidemia			
Yes	53	44	0.26
No	47	56	
Hypertension			
Yes	40	36	0.66
No	60	64	
Left ventricular hypertrophy			
Yes	11	15	0.53
No	89	85	
Diabetes mellitus			
Yes	34	23	0.12
No	66	77	

Immediate postoperative care of the patients was provided by the cardiac surgery intensive care unit (ICU) staff. Pericardial and pleural chest tube output was monitored frequently within the first few days after surgery and recorded in the patient's file. Extubated stable patients were transferred to the cardiac surgery step-down unit, usually on the second postoperative day.

The date of all transfusions was entered into the hospital central computer from the respective laboratories and this data was available by using the patients' hospital identification number. The use of red blood products or non-red blood products like fresh frozen plasma (FFP) and platelets was left to the surgical team's discretion.

Electrocardiograms (ECG) were recorded preoperatively and on the first to fifth days after surgery. Appearance of any new Qs wave in ECGs was recorded in the patient's file.

Cardiac enzyme marker (CK-MB) samples were collected preoperatively and at least five times during the first and second day after CABG. Cardiac enzyme marker more than 30

IU/L was considered for probable myocardial injury during CABG.

In all patients two-dimensional echocardiography was performed on the second and fifth day after CABG for detection of new regional wall motion abnormality (RWMA) in patients with new Qs wave on ECG or cardiac enzyme markers more than 30 IU/L. The primary study end points were in-hospital mortality, re-exploration rate, excessive pericardial and pleural tube bleeding and excessive requirements for red blood cells and non-red blood cell product requirements.

The study was also extended to evaluate preoperative aspirin use on perioperative myocardial infarction rate.

### Definitions

Definite perioperative myocardial infarction is defined as: new Qs wave on ECG and new RWMA on echo with or without CK-MB >30 IU/L and the definition of probable perioperative myocardial infarction is CK-MB >30 IU/L with new Qs on ECG or new RWMA on echo.<sup>13</sup>

### Statistical analysis

Statistical analysis was performed using SPSS® 11.5 (SPSS Inc., Chicago, IL, USA) for data storage and analysis. Continuous data were expressed as mean values  $\pm$ SD. Comparison of baseline categorical data was done by chi-square and continuous data by standard t-test. In all analyses with a 95% confidence interval (CI),  $P < 0.05$  was considered statistically significant.

### Results

One hundred (50%) individuals received aspirin and it was discontinued in the other group at least seven days before CABG. Neither the mean age nor sex was significantly different between the two groups. Patient's characteristics are summarized in Table I.

Aspirin users had more postoperative bleeding ( $608 \pm 359.7$  ml vs.  $483 \pm 251.5$  ml;  $P = 0.005$ ) and were transfused more red blood cell products ( $1.32 \pm 0.97$  units packed cells vs.  $0.94 \pm 1.02$  units packed cells;  $P = 0.008$ ) and fresh frozen plasma ( $2 \pm 1.84$  vs.  $1.46 \pm 1.64$ ;  $P = 0.03$ ) early after surgery, although platelet transfusion was not significantly different between groups ( $0.45 \pm 1.32$  vs.  $0.28 \pm 0.84$  units platelets,  $P = 0.25$ ). No in-hospital mortality was observed in the groups.

Regarding the secondary end points of the study, aspirin users had a significantly lower incidence of new Qs pattern on ECG after CABG (1% vs. 10%,  $P = 0.013$ ), but cardiac enzyme markers (CK-MB) and new regional wall motion abnormality (RWMA) were not different significantly between the two groups. (Table II).

There was no significant difference in the incidence of definite or probable perioperative myocardial infarction. Definite MI occurred in 0% of aspirin users vs. 3% of non-aspirin users ( $P = 0.24$ ) and probable MI occurred in 5% in group 1 vs. 8% in group 2, ( $P = 0.56$ ).

### Discussion

This study indicated that use of aspirin before CABG is associated with a higher risk of postoperative bleeding, with increased requirements for red blood cell products and fresh frozen plasma (FFP) transfusion. This finding was contradictory to other studies that showed patients receiving aspirin were no more likely to receive blood products.<sup>7-12</sup> Tuman and coworkers showed preoperative aspirin consumption dose not increase allogeneic blood transfusion in reoperative coronary artery surgery.<sup>7</sup> In another study, Vuylsteke et al. evaluated the effect of aspirin in coronary artery bypass grafting and they showed that aspirin therapy did not appear to increase blood loss, re-sternotomy for bleeding or blood products usage requirements during the hospital stay.<sup>8</sup> On the other hand, there are studies that confirm our finding.<sup>3-6</sup> Ferraris et al. evaluated aspirin and

postoperative bleeding after CABG. Their findings supported the hypothesis that aspirin is associated with a greater likelihood of postoperative bleeding.<sup>6</sup>

In our study, re-exploration rate for bleeding was 3% in each group, without significant difference (P=NS). Decey et al. found no significant difference in the rate of re-exploration for hemorrhage between patients who did and did not receive aspirin.<sup>10</sup> Another study confirmed that preoperative aspirin use had no effect on reexploration rate due to increased bleeding,<sup>8</sup> although Bashein et al. concluded that aspirin exposure within seven days before coronary bypass surgery is associated with an increased rate of reoperation for bleeding and that reoperation is associated with large increases in transfusion requirements and intensive care unit and hospital stays.<sup>5</sup> In the most recent study, Babee et al. showed aspirin usage within the five days preceding coronary artery bypass surgery is associated with a lower risk of postoperative in-hospital mortality and appears to be safe without an associated increased risk of reoperation for bleeding or need for blood product transfusions.<sup>14</sup>

Reductions in the rate of perioperative MI have been reported in aspirin users undergoing CABG. Klein et al. showed a reduction in the rate of perioperative myocardial infarction in patients receiving preoperative aspirin.<sup>11</sup> We evaluated the occurrence of definite perioperative MI and probable perioperative MI in the two groups. New Qs wave in ECG traces was significantly lower in aspirin users (P=0.013) but no significant difference was found for CK-MB rise or appearance of new RWMA (Table II). Risk of definite or probable perioperative MI was reduced with aspirin use before CABG, but did not achieve statistical significance.

**Table II. Perioperative myocardial infarction markers evaluation.**

Variable	Aspirin user	Non aspirin user	P-value
New QS pattern			
Yes	1	10	0.013
No	99	90	
Rise in CK-MB			
Yes	11	18	0.23
No	89	82	
New RWMA			
Yes	5	8	0.57
No	95	92	

### Limitations

This study was designed to evaluate aspirin's effect on postoperative bleeding. With respect to the fact that our study involves a small number of patients, therefore we might achieve statistical significance in the rate reduction of perioperative MI in larger groups.

### Conclusion

We found that aspirin use in patients undergoing elective CABG is associated with marked elevation in postoperative bleeding and requirements for red blood cells and FFP transfusion. We also found no significant reduction in the rate of definite or probable perioperative MI. Therefore we prefer to discontinue aspirin consumption for at least seven days before elective CABG surgery.

### References

1. Willard JE, Lange RA, Hillis LD. The use of aspirin in ischemic heart disease. *N Engl J Med* 1992; 327: 175-181.
2. Goldman S, Copeland J, Moritz T, Henderson W, Zadina K, Ovitt T. Long-term graft patency (3 years) after coronary artery surgery. Effects of aspirin: results of a VA Cooperative study. *Circulation* 1994; 89: 1138-1143.

3. Taggart DP, Siddiqui A, Wheatley DJ. Low-dose preoperative aspirin therapy, postoperative blood loss and transfusion requirements. *Ann Thorac Surg* 1990;50:424-428.
4. Kallis P, Tooze JA, Talbot S, Cowans D, Bevan DH, Treasure T. Preoperative aspirin decreases postoperative blood loss; a prospective, randomized, placebo-controlled, double-blind clinical trial in 100 patients with chronic stable angina. *Eur J Cardiothorac Surg* 1994; 8: 404-409.
5. Bashein G, Nessly ML, Rice AL, Counts RB, Misbach GA. Preoperative aspirin therapy and reoperation for bleeding after coronary artery bypass surgery. *Arch Intern Med* 1991; 151: 89-93.
6. Ferraris VA, Ferraris SP, Lough FC, Berry WR. Preoperative aspirin ingestion increases operative blood loss after coronary artery bypass grafting. *Ann Thorac Surg* 1998; 45: 71-74.
7. Tuman KJ, McCarthy RJ, O'Connor CJ, McCarthy WE, Ivanchovich AD. Aspirin does not increase allogeneic blood transfusion in reoperative coronary artery surgery. *Anesth Analg* 1996; 83: 1178-1184.
8. Vuylsteke A, Oduro A, Cardan E, Latimer RD. Effect of aspirin in coronary artery bypass grafting. *J Cardiothorac Vas Anesth* 1997; 11: 831-834.
9. Reich DL, Patel GC, Vela-Cantos F, Bodian C, Lansman S. Aspirin does not increase homologous blood requirements in elective coronary bypass surgery. *Anesth Analg* 1994; 79: 4-8.
10. Dacey LJ, Munoz JI, Johnson ER, Leavitt BJ, Maloney CT, Morton JR, Olmstead EM, Birkmeyer JD, O'Connor GT. Effect of preoperative aspirin use on mortality in coronary artery bypass grafting patients. *Ann Thorac Surg* 2001; 72; 1797-1798.
11. Klein M, Keith PR, Dauben HP, Schulte HD, Beckmann H, Mayer G, Elert O, Games E. Aprotinin counterbalances an increased risk of perioperative hemorrhage in CABG patients pretreated with aspirin. *Eur J Cardiothorac Surg* 1998; 14: 360-366.
12. Rawitscher RE, Jones JW, McCoy TA, Lindsley DA. A prospective study of aspirin's effect on red blood cell loss in cardiac surgery. *J Cardiovasc Surg (Torino)* 1991; 32: 1-7.
13. Adams DH, Antman EM. Medical management of the patient undergoing cardiac surgery. In: Branwald E, Zipes DP, Libby P, (eds). *Heart Disease, A Textbook Cardiovascular Medicine*. 6<sup>th</sup> eds. Philadelphia, W. B. Saunders Company, 2001, p. 2070.
14. Babee KA, Powell PD, Valeti U, Rosales G, Kopecky SL, Mullany C, Wright S. Preoperative aspirin therapy is associated with improved postoperative outcomes in patients undergoing coronary artery bypass grafting. *Circulation* 2005; 112: 286-292.