

# The effect of preoperative aspirin use on postoperative bleeding and perioperative myocardial infarction in patients undergoing coronary artery bypass surgery

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## Abstract

**Background:** We tried to evaluate the clinical outcomes (mortality, postoperative bleeding and perioperative myocardial infarction) of 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 and divided into two groups. One group received aspirin 80–160 mg, while in the other aspirin was stopped at least seven days before surgery. The primary end-points of the study were in-hospital mortality and hemorrhage-related complications (postoperative blood loss in the intensive care unit, re-exploration for bleeding and red blood cell and non-red blood cell requirements). The secondary end-point was perioperative myocardial infarction.

**Results:** There were no differences in patient characteristics between the 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 ( $1.32 \pm 0.97$  unit packed cell vs.  $0.94 \pm 1.02$  unit packed cell;  $p = 0.008$ ). There was no significant difference between the two groups regarding platelet requirement and the rate of in-hospital mortality and re-exploration 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) or in-hospital mortality between the two groups.

**Conclusion:** Preoperative aspirin administration increased postoperative bleeding and red blood cell requirements with no effect on mortality, re-exploration rate and perioperative myocardial infarction. We recommend withdrawal of aspirin seven days prior to surgery. (Cardiol J 2007; 14: 453–457)

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

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Received: 10.05.2007

Accepted: 19.07.2007

## Introduction

Aspirin is an effective therapy in the management of stable and unstable coronary artery disease [1]. Early initiation of aspirin after coronary artery bypass graft (CABG) surgery reduces the risk of graft occlusion [2]. Aspirin has been implicated in platelet dysfunction and prolongation of bleeding time, but its effect on postoperative bleeding, re-exploration and blood-product requirement is controversial [3–12]. In this study we tried to determine the 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 200 patients (67 aspirin users were male *vs.* 70 non-aspirin users,  $p = 0.761$ ; mean age was  $56.9 \pm 9.14$  years in aspirin users *vs.*  $56.9 \pm 9.59$  years in non-aspirin users,  $p = 0.83$ ), who underwent CABG surgery in our cardiovascular surgery department between November 2005 and December 2006. We received ethical approval for the study and the patients gave their informed written consent to participation in the study. We included patients who were undergoing elective CABG for the first time. Our exclusion criteria were: 1) the need for concomitant valvular, aortic or aneurysmectomy surgery; 2) concomitant antiplatelet drug consumption, including clopidogrel, ticlopidin, glucocorticoides, non-steroid anti-inflammatory drugs. We used the left internal mammary artery as a graft. The total number of grafts was below five and all the operations were performed by a single surgical team. Patient characteristics are summarized in Table 1.

The patients were randomly assigned into one of two groups. Group 1 received aspirin preoperatively while in Group 2 aspirin was stopped at least seven days before CABG. All patients received a single dose of aprotinin (2,000,000 kallikrein inhib-

itor units) once during surgery. Aspirin was started post-operatively within 6 h of CABG in both groups.

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

The dates of all transfusion information were entered into the hospital central computer from the respective laboratories and these data were made available by the use of the patient hospital identification numbers. The use of red blood products or non-red blood products such as fresh frozen plasma (FFP) and platelets was at the discretion of the surgical team.

ECGs were recorded preoperatively and on the first to fifth days after CABG. New QS waves on ECG were recorded in the patients' files.

Cardiac enzyme marker (CK-MB) samples were collected preoperatively and at least five times during the first and second day after CABG. A CK-MB of more than 30 IU/L was suspicious for myocardial injury during CABG.

In all patients two-dimensional echocardiography was performed on the second and fifth days after CABG for detection of new regional wall motion abnormality (RWMA) in patients with a new QS on ECG or CK-MB of more than 30 IU/L. The primary study end-points were hospital mortality, re-exploration, excessive pericardial and pleural tube bleeding and an excessive requirement for red blood cell and non-red blood cell products.

The study was also extended to examine the effect of preoperative aspirin prescription on the rate of perioperative MI.

## Definitions

Definite perioperative MI was defined by a new QS on ECG and a new RWMA on ECHO with or without CK-MB > 30 IU/L, and the definition of

**Table 1.** Patient characteristics.

Variables	Aspirin user (n = 100)	Non-aspirin user (n = 100)	p
Left ventricular ejection fraction	41.7 ± 11.6	42.6 ± 11.3	0.69
Cigarette smokers	36 (36%)	36 (36%)	1.00
Dyslipidemic patients	53 (53%)	44 (44%)	0.26
Hypertensive patients	40 (40%)	36 (36%)	0.66
Presence of left ventricular hypertrophy	11 (11%)	15 (15%)	0.53
Diabetic patients	34 (34%)	23 (23%)	0.12

P value < 0.05 is significant.

probable perioperative MI was CK-MB > 30 IU/L with a new QS on ECG or a new RWMA on ECHO [13].

### 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 value ± SD. Comparison of baseline categorical data was performed by the  $\chi^2$  test and continuous data were compared by a standard t-test. In all analyses with a 95% confidence interval (CI),  $p < 0.05$  was considered statistically significant.

### Results

One hundred (50% of the total) individuals received aspirin, whereas this was discontinued in the other group for at least seven days before CABG. There were no significant differences between the two groups in terms of mean age or sex. The patients' characteristics are summarized in Table 1.

The aspirin users had more post-operative bleeding ( $608 \pm 359.7$  ml *vs.*  $483 \pm 251.5$  ml;  $p = 0.005$ ) and received more red blood cell products ( $1.32 \pm 0.97$  unit packed cell *vs.*  $0.94 \pm 1.02$  unit packed cell;  $p = 0.008$ ) and FFP ( $2 \pm 1.84$  *vs.*  $1.46 \pm 1.64$ ;  $p = 0.03$ ) early after surgery, although platelet transfusion was not significantly different between the two groups ( $0.45 \pm 1.32$  *vs.*  $0.28 \pm 0.84$  unit platelet,  $p = 0.25$ ). No in-hospital mortality was observed in either group.

With regard to the secondary end-points of the study, the aspirin users had a significantly lower incidence of new QS patterns on ECG after CABG (1% *vs.* 10%;  $p = 0.013$ ), but CK-MB and RWMA did not differ significantly between the two groups (Table 2).

There was no significant difference in the incidence of definite or probable perioperative MI.

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 the use of aspirin before CABG is associated with a higher risk of postoperative bleeding and an increased requirement for red blood cell products and FFP transfusion. This finding was counter to other studies, which showed that patients receiving aspirin were no more likely to receive blood products [7–12]. Tuman et al. [8] showed that preoperative aspirin consumption does not increase allogeneic blood transfusion in reoperative coronary artery surgery. In another study, Vuylsteke et al. [9] evaluated the effect of aspirin in coronary artery bypass grafting and showed that aspirin therapy did not appear to increase blood loss, reopening for bleeding or blood product usage requirements during the hospital stay. On the other hand, there are studies that confirm our finding [3–6]. Ferraris et al. [6] evaluated aspirin and postoperative bleeding after CABG. Their findings support the hypothesis that aspirin is associated with a greater likelihood of postoperative bleeding. Recently Ferraris et al. wrote in clinical practice guidelines that it was reasonable to discontinue low intensity antiplatelet drugs such as aspirin only in purely elective patients without acute coronary syndromes before surgery in the expectation that blood transfusion will be reduced (Class II A, level of evidence A) [7].

In our study the re-exploration rate for bleeding was 3% in each group without significant differences ( $p = \text{NS}$ ). Dacey et al. [11] found no significant difference in the rate of re-exploration for hemorrhage between patients who had and those who had not received aspirin. Other studies

**Table 2.** Evaluation of perioperative myocardial infarction markers.

Variables	Aspirin user (n = 100)	Non-aspirin user (n = 100)	p
<b>New QS pattern</b>			
Yes	1 (1%)	10 (10%)	0.013
No	99 (99%)	90 (90%)	0.013
<b>Rising CK-MB marker</b>			
Yes	11 (11%)	18 (18%)	0.23
No	89 (89%)	82 (82%)	0.23
<b>New RWMA</b>			
Yes	5 (5%)	8 (8%)	0.57
No	95 (95%)	92 (92%)	0.57

confirmed that pre-surgery aspirin prescription has no effect on the re-exploration rate due to increased bleeding [9], although Bashein et al. [5] concluded that aspirin exposure within seven days of 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 ICU and hospital stays. In the most recent study Bybee et al. [15] showed that aspirin usage within the five days preceding CABG is associated with a lower risk of post-operative in-hospital mortality, appears to be safe and is not associated with any increased risk of reoperation for bleeding or the need for blood product transfusion.

A reduction in the rate of perioperative MI has been reported in aspirin users undergoing CABG. Klein et al. [12] showed a reduction in the rate of perioperative MI in patients receiving preoperative aspirin. We evaluated the occurrence of definite perioperative MI and probable perioperative MI in two groups. New QS waves on ECG were significantly lower in aspirin users ( $p = 0.013$ ), but no significant difference was found for an increase in CK-MB or the appearance of new RWMA (Table 2). The risk of definite or probable perioperative MI was reduced with aspirin use before CABG but did not achieve statistical significance.

### Study limitations

This study was designed for evaluation of the effect of aspirin on postoperative bleeding and involved a small number of patients. In larger groups we might therefore achieve statistical significance in the rate of reduction of perioperative MI.

### Conclusions

We found that aspirin use in patients undergoing elective coronary artery bypass graft surgery is associated with a marked elevation in postoperative bleeding and the need for red blood cell and fresh frozen plasma transfusion. We also found no significant reduction in the rate of definite or probable perioperative MI. We therefore prefer to discontinue aspirin consumption for at least seven days before elective CABG.

### 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 post-operative 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. The Society of Thoracic Surgeons Blood Conservation Guideline Task Force: Ferraris VA, Ferraris SP, Saha SP, Hessel II EA, Haan CK, Royston BD, Bridges CR, Higgins RSD, Despotis G, Brown JR; The Society of Cardiovascular Anesthesiologists Special Task Force on Blood Transfusion: Spiess BD, Shore-Lesserson L, Stafford-Smith MC, Mazer D, Bennett-Guerrero E, Hill SE, Body S. Perioperative Blood Transfusion and Blood Conservation in Cardiac Surgery: The Society of Thoracic Surgeons and The Society of Cardiovascular Anesthesiologists Clinical Practice Guideline. *Ann Thorac Surg*, 2007; 83: S27–S86.
8. Tuman KJ, McCarthy RJ, O'Connor CJ, McCarthy WE, Ivanchovich AD. Aspirin dose not increase allogeneic blood transfusion in reoperative coronary artery surgery. *Anesth Analg*, 1996; 83: 1178–1184.
9. Vuylsteke A, Oduro A, Cardan E, Latimer RD. Effect of aspirin in coronary artery bypass grafting. *J Cardiothorac Vas Anesth*, 1997; 11: 831–834.
10. 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.
11. Dacey LJ, Munoz JI, Johnson ER et al. Effect of preoperative aspirin use on mortality in coronary artery bypass grafting patients. *Ann Thorac Surg*, 2001; 72: 1797–1798.
12. Klein M, Keith PR, Dauben HP et al. Aprotinin counterbalances an increased risk of peri-operative hemorrhage in CABG patients pretreated with aspirin. *Eur J Cardiothorac Surg*, 1998; 14: 360–366.

13. 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.
14. Adams DH, Antman EM. Medical management of the patient undergoing cardiac surgery: In: Braunwald E, Zipes DP, Libby P (eds.) *Heart disease. A textbook of cardiovascular medicine*. 6<sup>th</sup> eds. W.B. Saunders, Philadelphia 2001: 2070.
15. Bybee 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. *Circ* 2005; 112: 286-292.