The Heart Surgery Forum #2010-1087
14 (1), 2011 [Epub February 2011]
doi: 10.1532/HSF98.20101087

Online address: http://cardenjennings.metapress.com

Practice Considerations of Early Aspirin Administration following Coronary Artery Bypass Surgery

Dr. Gukop

Philemon Gukop, Nicholaos Kakouros, Morteza Tavakkoli Hosseini, Oswaldo Valencia, Antonios Kourliouros, Mazin Sarsam, Venkatachalam Chandrasekaran

Department of Cardiothoracic Surgery, St. George's Hospital, London, UK

ABSTRACT

Thrombotic occlusion of saphenous vein grafts (SVG), the conduits most commonly used in coronary artery bypass grafting (CABG) surgery, causes significant morbidity and mortality. There is class 1A evidence that early aspirin administration following CABG reduces thrombotic SVG occlusion, as well as overall morbidity and mortality. The American Heart Association/American College of Cardiology and the European Association of Cardiothoracic Surgeons have issued guidelines recommending that 150 to 325 mg aspirin be administered within 6 hours following CABG. We carried out a clinical audit of our practice to identify any reasons for deviation from these standards of care and to implement any corrective measures. We prospectively collected data on 200 consecutive patients who underwent CABG to assess both the compliance in prescribing and administering aspirin and the effect on blood loss and transfusion requirements. Sixty-nine percent of patients received an aspirin loading dose 6 hours postoperatively. The reasons for nonadministration of aspirin were postoperative bleeding (10%), lack of a prescription despite aspirin being clinically indicated (13%), and a prescription for aspirin but no administration (9%). Reasons included inadequate handover between clinical teams (4%), aspirin loading ≤24 hours preoperatively (2%), and administration after the first 6 hours (3%). Our audit showed that early aspirin administration did not cause further bleeding or increase blood or blood product transfusion. We followed the recommendations in the majority of cases, but there is scope for improvement in this practice and a need to address "gray areas" not covered by the guidelines.

INTRODUCTION

Saphenous vein graft (SVG) occlusion constitutes a significant source of morbidity and mortality following coronary artery bypass grafting (CABG). Its pathogenesis is not completely understood, but the factors implicated include thrombosis, yellow plaque formation, SVG spasm, small caliber of the grafted vessel (≤2.0 mm), and neointima formation/vascular smooth muscle cell proliferation [Shukla 2003; Hata 2007]. Studies have shown that low-dose aspirin administered early in the postoperative period plays a significant role in preventing or at least reducing the incidence of SVG occlusion [Goldman 1988; Gavaghan 1991]. Early administration of aspirin following SVG surgery with continued indefinite use has been shown to significantly improve morbidity and mortality [Gavaghan 1991; Mangano 2002]. There is no evidence for an improved patency of arterial grafts with aspirin, so although long-term aspirin therapy is recommended for this group of patients to improve the outcomes of their atherosclerotic disease, its commencement could be deferred until after the acute postoperative period.

The American Heart Association (AHA)/American College of Cardiology (ACC), the American College of Chest Physicians, and the European Association of Cardiothoracic Surgeons (EACTS) have issued guidelines for the administration of aspirin within 24 hours after SVG surgery [Eagle 2004; Stein 2004; Dunning 2008]. Best results are obtained when aspirin is administered within 6 hours postoperatively [Fremes 1993]. The guidelines strongly recommend that a fail-safe mechanism be in place to ensure that aspirin is administered early when saphenous veins are used as graft conduits [Eagle 2004; Dunning 2008]. We have taken these evidence-based recommendations to set standards of care and have audited the practice in the Cardiothoracic Surgery Department at St George's Hospital, London, against these standards.

Our institutional policy is to administer 300 mg of aspirin within 6 hours after CABG in the absence of significant postoperative bleeding (ie, ≥200 mL/hour for >3 consecutive hours). This policy includes all CABG patients, including those who have received arterial grafts only. We elected to perform this audit of our practice to identify areas of discrepancy with recommendations, assess practical implications of the guidelines, and recommend corrective measures.

MATERIALS AND METHODS

We prospectively collected and evaluated data from 200 consecutive patients who underwent urgent or elective

Received June 29, 2010; received in revised form August 13, 2010; accepted August 18, 2010.

Correspondence: Venkatachalam Chandrasekaran, FRCS, Department of Cardiothoracic Surgery, St. George's Hospital, Blackshaw Rd, London SW17 0QT, UK; +44-2087253962; fax: +44-2087252170 (e-mail: v.chandrasekaran@stgeorges.nhs.uk).

Table 1. Patient Demographic Data and Preoperative Characteristics*

Variable	Early Aspirin Administered (n = 137)	Early Aspirin Not Administered (n = 63)	*P*
Male sex, n	106 (77)	49 (78)	.95
Age, y	69 (63-67)	73 (64-77)	.04
Body mass index, kg/m^2	28 (26-32)	27 (24-29)	.04
EuroSCORE	2.7 (1.6-4.2)	3.3 (2.1-6.4)	.07
Smoking, n (%)	79 (58)	29 (46)	.13
Diabetes, n (%)	26 (19)	13 (20)	.78
Hypertension, n (%)	97 (71)	46 (73)	.75
Renal disease, n (%)	1 (1)	1 (2)	.53
Pulmonary disease, n (%)	11 (8)	9 (14)	.17
Neurologic disease, n (%)	13 (10)	1 (2)	.07
Carotid bruit, n (%)	12 (9)	8 (13)	.39
Arteriopathy, n (%)	7 (5)	5 (8)	.52
LVEF <50%, n (%)	25 (18)	14 (22)	.51
Recent MI (<30 d), n (%)	22 (35)	10 (36)	.94
Previous MI, n (%)	63 (46)	28 (44)	.84
Previous PCI, n (%)	12 (9)	6 (10)	.86
CCS grade III-IV, n (%)	32 (23)	15 (24)	.64
NYHA grade III-IV, n (%)	16 (12)	4 (6)	.27

*Categorical data are presented as number (percent); continuous data with a nonnormal distribution are presented as the median (interquartile range). LVEF indicates left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention; CCS, Canadian Cardiovascular Society; NYHA, New York Heart Association.

Table 2. Preoperative Medication History*

Variable	Early Aspirin Administered (n = 137)	Early Aspirin Not Administered (n = 63)	*P*
Aspirin use, n (%)	128 (93)	51 (81)	<.01
Clopidogrel use, n (%)	46 (34)	28 (44)	.14
β-Blocker use, n (%)	98 (72)	42 (67)	.49
ACEI use, n (%)	103 (75)	40 (64)	.09
Aspirin stopped preoperatively, d	7 (6-7)	7 (3-7)	.10
Clopidogrel stopped preoperatively, d	7 (5-7)	7 (3-8)	.78
ACEI stopped preoperatively, d	4 (4-5)	4 (2-5)	.08

*Categorical data are presented as number (percent); continuous data with a nonnormal distribution are presented as the median (interquartile range). ACEI indicates angiotensin-converting enzyme inhibitor.

Table 3. Intraoperative Variables*

Variable	Early Aspirin Administered (n = 137)	Early Aspirin Not Administered (n = 63)	*P*
LIMA, n (%)	121 (88)	57 (91)	.65
Radial artery graft, n (%)	42 (31)	18 (29)	.76
SVG, n (%)	128 (93)	52 (83)	.02
CPB use, n (%)	107 (78)	53 (84)	.32
CPB time, min	94 (78-120)	96 (70-125)	.95
Cross-clamp time, min	66 (50-88)	63 (49-94)	.86

*Categorical data are presented as number (percent); continuous data with a nonnormal distribution are presented as the median (interquartile range). LIMA indicates left internal mammary artery; SVG, saphenous vein graft; CPB, cardiopulmonary bypass.

CABG, with and without the use of cardiopulmonary bypass, between April and September 2009. Preoperative variables of interest included medical and drug history, particularly prior use of antiplatelet agents. Primary outcomes of interest were whether aspirin was prescribed, whether it was administered in the early postoperative period, and if not, for what reason. We also evaluated outcomes that could be influenced by aspirin treatment, such as postoperative bleeding, blood and blood product requirements, and reoperation for bleeding.

Statistical Analysis

Dichotomous data were evaluated with the Pearson chi-square test or the Fisher exact test, whereas continuous variables with a nonnormal distribution were evaluated with the Mann-Whitney *U* test. A *P* value <.05 was considered statistically significant. Results are presented as the median and interquartile range (IQR) for continuous variables with a nonnormal distribution. Statistical analysis was performed with the SPSS software package (version 17.0; SPSS, Chicago, IL, USA).

RESULTS

Of the 200 evaluated patients, 137 (69%) received early aspirin (defined as administration 6 hours postoperatively), and 63 (31%) did not. Tables 1, 2, and 3 summarize the characteristics and medical and drug histories of the patients, as well as the procedural variables for the patients who received early aspirin and those who did not.

Of the 180 patients who received at least 1 SVG (90%), 128 patients (71%) received early aspirin. Nine (45%) of the 20 patients who had totally arterial grafts also received early aspirin. Of the total of 200 patients, 19 (10%) did not receive early aspirin because of significant bleeding (≥200 mL/hour for >3 consecutive hours, in accordance with our local protocol) (Figure 1), whereas 26 patients (13%) did not receive early aspirin because it had not been prescribed. Nonprescription was due to a history of allergy or an adverse reaction to aspirin in 3 patients; in the remaining 23 patients (12%), the reason for omission was not documented in the notes (Figure 1).

In the remaining 18 patients (9%), aspirin prescription was indicated on the drug chart but was not administered, for a variety of reasons (Figure 1). In 4 of these 18 patients, aspirin prescribed by the junior doctor in the operating room was

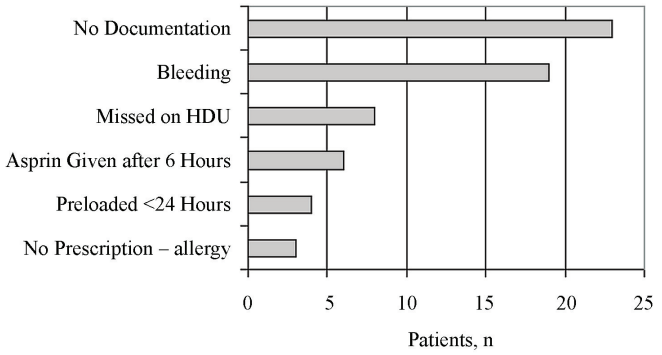

Figure 1. Reasons for not administering aspirin early (n = 63). HDU indicates high dependency unit.

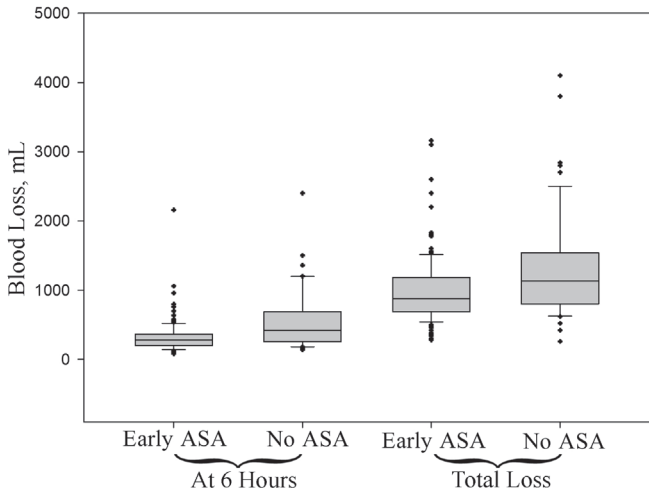

Figure 2. Drain output at 6 hours and total drain output in patients who received early aspirin (ASA) versus those who did not.

revoked by the more senior cardiothoracic registrar prior to administration. These patients had been loaded with aspirin or clopidogrel ≤24 hours before surgery, either as part of the acute coronary syndrome protocol or for a previous percutaneous intervention, and then required urgent surgery. For this category of patients, there is no clear recommendation as to whether they ought to be reloaded within 6 hours following CABG using an SVG. In 8 of these 18 patients, nonadministration was due to inadequate handover during patient transfer from the intensive care unit (ICU) to the high dependency unit (HDU), such that the prescribed loading dose of aspirin was not given in the ICU but the prescription was then not transcribed onto the new HDU drug chart (our local policy is to use different drug charts in the ICU and the HDU). The remaining 6 patients received the prescribed aspirin later than 6 hours after the CABG operation. Patients who were not prescribed a loading dose of aspirin in the early postoperative period did not subsequently receive a delayed loading dose but instead were commenced directly to receive a maintenance dose of 75 mg.

Table 4. Postoperative Variables and Blood Loss*

Variable	Early Aspirin Administered (n = 137)	Early Aspirin Not Administered (n = 63)	*P*
Resternotomy, n (%)	4 (3)	6 (10)	.08
Dialysis, n (%)	1 (1)	2 (3)	.23
IABP, n (%)	1 (1)	1 (2)	.53
ICU stay, d	1 (0-1)	1 (1-2)	.02
Postoperative stay, d	5 (5-7)	6 (5-9)	.04
IABP use, n (%)	1 (1)	1 (2)	.53
Drain output 200 mL/h, n (%)	8 (6)	19 (30)	<.001
Drain output at 6 h postoperatively, mL	280 (200-360)	420 (260-675)	<.001
Total drain output, mL	880 (700-1180)	1130 (800-1540)	.005

*Categorical data are presented as number (percent); continuous data with a nonnormal distribution are presented as the median (interquartile range). IABP indicates intra-aortic balloon pump; ICU, intensive care unit.

Our audit showed that postoperative bleeding (≥200 mL/hour) often occurred in patients who did not receive early aspirin (30% versus 6%, $P < .001$; Table 4). This finding is consistent with our policy that suggests that patients with significant bleeding should not receive loading aspirin. There was no evidence that early aspirin loading increased the risk of bleeding, because the 6-hour and total drain outputs were higher for those who did not receive early aspirin (Figure 2). It is apparent, however, that the decision to administer aspirin in this population was based on the absence of significant postoperative bleeding, a practice that introduces a potent selection bias.

In addition, the difference in resternotomy rates between the patients who received early aspirin and those who did not was not significant (3% versus 10%, $P = .08$). This finding is similar to that of a previous study, which showed a higher but statistically insignificant resternotomy rate in those who received early aspirin [Gavaghan 1991]. Once again, given the difference in selection bias between the 2 groups, the patients who received aspirin and those who did not showed no significant difference in the postoperative use of blood and blood products (Table 5).

Interestingly, despite the lack of a significant difference in the proportion receiving early aspirin, patients who underwent on-pump CABG were more likely to require blood transfusion ($P < .05$, Table 6). This result is likely related to the higher heparin dose used in on-pump CABG, as well as to pump-induced coagulopathy [Casati 2001].

DISCUSSION

The ACC/AHA and EACTS guidelines recommend that aspirin be administered within 6 hours following CABG for the optimal prevention of thrombotic SVG occlusion and

Table 5. Transfusion and Other Procoagulation Measures

Variable	Early Aspirin Administered (n = 127)	Early Aspirin Not Administered (n = 63)	*P*
Intraoperative blood transfusion, n (%)	14 (10)	5 (8)	.61
Thromboelastogram, n (%)	15 (11)	23 (37)	<.001
Platelet transfusion, n (%)	18 (13)	24 (38)	<.001
Fresh frozen plasma, n (%)	16 (12)	21 (33)	<.001
Postoperative blood transfusion 4 units, n (%)	2 (1)	9 (14)	.002
Tranexamic acid use, n (%)	13 (9)	11 (18)	.11
Protamine top-up, n (%)	8 (6)	16 (25)	<.001

Table 6. Comparison of Patients Having On-Pump and Off-Pump Coronary Artery Bypass Grafting (CABG)

Variable	Off-Pump CABG (n = 40)	On-Pump CABG (n = 160)	*P*
Early aspirin administered, n (%)	30 (75)	107 (67)	.32
Intraoperative blood transfusion, n (%)	1 (3)	18 (11)	.13
Postoperative blood transfusion, n (%)	5 (13)	67 (42)	<.05
Resternotomy for bleeding, n (%)	1 (3)	9 (6)	.69
Drain output at 6 h postoperatively, mL	327	412	.80
Total drain output, mL	967	1109	.51

that it be administered continuously thereafter. A loading dose of 150 to 325 mg at 6 hours is recommended, followed by 75 to 162 mg/day [Musleh 2003]. These recommendations are based on observational studies, randomized controlled trials, and meta-analyses, which have shown the important effect of early aspirin administration on SVG patency. The best results have been demonstrated when aspirin was administered within 1 hour postoperatively [Gavaghan 1991]. No study has reported increased bleeding caused by early aspirin administration [Dunning 2008]. The standard of care, therefore, is to administer aspirin within the first 6 hours after SVG surgery.

It is not uncommon for routine clinical practice to deviate from published recommendations. Such deviations, however, may be appropriate or accounted for in some cases. Deviation may occur, for example, in "gray cases" in which the guidelines are unclear regarding the recommended practice. Our audit showed that 4 patients did not receive an early aspirin loading dose because they had been preloaded with aspirin ≤24 hours before surgery as part of an acute coronary syndrome protocol or for a coronary artery angiogram. Guidelines are unclear as to whether a postoperative loading dose of aspirin is required for patients who received aspirin <24 hours preoperatively. The residents on call used their discretion to withhold further aspirin loading in these cases, but there is no clear policy for this category of patients. Our recommended practice in patients who have been preloaded with aspirin (300 mg in ≤24 hours) and those receiving aspirin until the day of surgery is to not provide further loading but to administer the usual daily dose of aspirin instead. This practice is based on the fact that aspirin irreversibly inhibits cyclooxygenase and that loading saturates 50% to 80% of the protein-binding capacity. These patients therefore should require only a daily maintenance dose to sustain the free active aspirin in the serum.

Another potential cause for deviation from published standards was lack of awareness or suboptimal communication. Thirty-one patients (16%) did not receive early aspirin because of handover-related problems. More specifically, in 23 cases in which aspirin was not prescribed and therefore not given, the lack of administration took place during the changeover period for junior doctors. In 8 patients, aspirin was not administered, even though it was prescribed on the ICU chart, because of a failure to transcribe the prescription to the separate HDU chart when the patient was moved to the HDU. This failure occurred when it was unclear whether the surgical team or the intensive therapy unit team was responsible for prescribing the postoperative medication. To prevent such failures, we recommend that the importance of early aspirin administration be emphasized to new staff at their induction and be specifically discussed as part of a patient's handover during shift changes or the patient's transfer from the ICU to the HDU. Since this audit, our practice has changed so that the postoperative drug is scripted by the surgical team and checked in the operating room as part of the stage 3 World Health Organization Surgical Safety Checklist [Senior 2009].

Aspirin was not administered to 3 of our patients because of a previous history of allergy or adverse reaction to aspirin. These patients received no alternative antiplatelet agent. Clopidogrel should be used as an alternative, as emphasized in the ACC/AHA guideline for true aspirin allergy [Eagle 2004].

Our audit showed that patients who did not receive early aspirin because of bleeding (as recommended by our hospital protocol) had a higher median age (73 years [IQR, 64-77 years] versus 69 years [IQR, 63-74 years]; $P = .04$) and a higher median EuroSCORE (3.3 [IQR, 2.1-6.4] versus 2.7 [IQR, 1.6-4.2]; $P = .07$]. These patients therefore belonged to a higher-risk category, although the results were not statistically significant. Nonetheless, because the evidence is overwhelming that early aspirin is beneficial and does not increase the risk of postoperative bleeding, these categories of patients (elderly, higher EuroSCORE) should not be denied the benefit of early aspirin. In cases of moderate nonsurgical bleeding, there is still a place for early aspirin administration except when the thromboelastogram shows platelet dysfunction. In such cases, aspirin administration can be delayed until bleeding has decreased to a reasonable level.

Despite the fact that studies have not demonstrated any protective benefit of early aspirin on arterial graft occlusion

[Eagle 2004], we recommend early aspirin administration for all patients after CABG because of its simplicity and its potential to significantly reduce the incidence of subsequent mortality, myocardial infarction, stroke, renal failure, and bowel infarction [Fremes 1993]. Once again, the aforementioned relevant recommendations do not specify the subgroup of patients who received totally arterial revascularization because there is lack of adequate evidence on the timing of first-dose aspirin. We strongly recommend that consultant approval be required for withholding early aspirin following CABG to ensure that the risk-benefit ratio has been adequately evaluated.

Although we mostly follow published standards, there is still scope for improvement of practice. We anticipate that our suggestions will help address gray areas not covered by the guidelines and will encourage better practice.

REFERENCES

Casati V, Gerli C, Franco A, et al. 2001. Activation of coagulation and fibrinolysis during coronary surgery: on-pump versus off-pump techniques. Anesthesiology 95:1103-9.

Dunning J, Versteegh M, Fabbri A, et al. 2008. Guideline on antiplatelet and anticoagulation management in cardiac surgery. Eur J Cardiothorac Surg 34:73-92.

Eagle KA, Guyton RA, Davidoff R, et al. 2004. ACC/AHA 2004 guideline update for coronary artery bypass graft surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1999 Guidelines for Coronary Artery Bypass Graft Surgery). Circulation 110:e340-437.

Fremes SE, Levinton C, Naylor CD, Chen E, Christakis GT, Goldman BS. 1993. Optimal antithrombotic therapy following aortocoronary bypass: a meta-analysis. Eur J Cardiothorac Surg 7:169-80.

Gavaghan TP, Gebski V, Baron DW. 1991. Immediate postoperative aspirin improves vein graft patency early and late after coronary artery bypass graft surgery. A placebo-controlled, randomized study. Circulation 83:1526-33.

Goldman S, Copeland J, Moritz T, et al. 1988. Improvement in early saphenous vein graft patency after coronary artery bypass surgery with antiplatelet therapy: results of a Veterans Administration Cooperative Study. Circulation 77:1324-32.

Hata M, Sezai A, Niino T, et al. 2007. What is the optimal management for preventing saphenous vein graft diseases?: early results of intravascular angioscopic assessment. Circ J 71:286-7.

Mangano DT. 2002. Aspirin and mortality from coronary bypass surgery. N Engl J Med 347:1309-17.

Musleh G, Dunning J. 2003. Does aspirin 6 h after coronary artery bypass grafting optimise graft patency? Interact Cardiovasc Thorac Surg 2:413-5.

Senior K. 2009. WHO Surgical Safety Checklist has value worldwide. Lancet Infect Dis 9:211.

Shukla N, Angelini GD, Ascione R, Talpahewa S, Capoun R, Jeremy JY. 2003. Nitric oxide donating aspirins: novel drugs for the treatment of saphenous vein graft failure. Ann Thorac Surg 75:1437-42.

Stein PD, Schunemann HJ, Dalen JE, et al. 2004. Antithrombotic therapy in patients with saphenous vein and internal mammary artery bypass grafts: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 126(suppl):600S-8S.