Impact of clopidogrel antiplatelet therapy on surgical outcome in selected patient populations

Mohamed A. Alrabiey, Ehab Said and Ehab El-Shahat

Department of Anesthesiology, Faculty of Medicine, Benha University, Benha City, Egypt

Correspondence to Mohamed Al-Rabiey, MD, Department of Anesthesiology, Faculty of Medicine, Benha University, 13111 Benha City, Egypt
Tel: +002 011 4424 4462/002 010 2050 3009; e-mail: ashrafrabiey@yahoo.com

Received 23 March 2012
Accepted 16 June 2012

Ain-Shams Journal of Anesthesiology
2012, 5:333–338

Objectives
The aim of the study is to evaluate the impact of antiplatelet therapy (APT) on surgical outcome of patients requiring emergency surgery while on APT and on that of patients assigned for elective surgery and had stopped their APT for 1 week before surgery.
Patients and methods
This selective study included 30 patients on aspirin alone (ASP group), 30 patients on clopidogrel alone (CLO group), and 30 patients receiving both (combination group); in addition, 30 patients without any history of APT (control group) and 30 patients on combined APT and assigned to elective major surgeries who discontinued APT for 7 days before surgery were also included.
Results
The study included 150 patients with a mean age of 59.6 ± 7.3 years; range: 43–78 years. Patients who received APT showed significantly greater amounts of blood loss during and at 12 h after surgery, with a concomitantly significantly higher number of blood units consumed compared with the control group. Patients of the CLO group showed the least deviation from the elective group. The combination group showed significantly greater blood loss and a higher need for blood transfusion compared with both the CLO and the elective group. Patients of the ASP group showed significantly higher blood loss and more need for transfusion therapy compared with the elective group.
Conclusion
Elective stoppage of APT for 7 day before surgery, if not hazardous, is advisable. Emergency surgical procedure for patients maintained on chronic APT is not so harmful despite the increased need for transfusions, but the outcome is best in those receiving CLO alone.

Keywords:
antiplatelet therapy, continue, elective surgery, emergency surgery, stop

Ain-Shams J Anesthesiol 5:333–338

1687-7934

Introduction

Thienopyridine clopidogrel is an antiplatelet drug known to work by noncompetitive inhibition of the platelet ADP receptor (P2Y12), resulting in reduced platelet aggregation. Acetylsalicylic acid (aspirin) is a noncompetitive, irreversible antagonist of the enzyme cyclooxygenase-1 that inhibits the synthesis of prostaglandins and thromboxane A_2 from arachidonic acid. Reduced concentrations of thromboxane A_2 lead to inhibition of platelet aggregation and adhesiveness [1–3].

The use of platelet aggregation inhibitors, including aspirin, glycoprotein IIb/IIIa inhibitors, and clopidogrel, has become a standard management strategy for patients with acute coronary syndrome. Clopidogrel significantly reduced the risk of cardiovascular death, myocardial infarction, stroke, and other related ischemic events in these patients. Clopidogrel demonstrated benefits incremental to and independent of other therapeutic agents, including anticoagulants, angiotensin-converting enzyme inhibitor blockers, and lipid-lowering agents. Clopidogrel treatment may also be beneficial for patients who have not had the opportunity to undergo coronary angiography with subsequent percutaneous coronary intervention and are dependent on thrombolytic therapy, as well as those who require urgent surgical revascularization [4–6].

The well-documented efficacy of both aspirin and clopidogrel as antiplatelet therapies, either alone or in combination, leads to a progressive increase in their use in chronic therapy; however, concerns arose with regard to the tendency of these patients to bleed during an emergency surgical procedure, especially if there is blood loss secondary to the trauma. Another point of debate of whether to stop or continue the antiplatelet therapy (APT) arose for patients maintained on chronic APT and admitted for major elective surgery, such as joint replacement surgeries, cancer, and vascular surgeries, especially if associated with blood loss [7–9]. Thus the current study aimed to evaluate the impact of APT on surgical outcome of patients requiring emergency surgery while

DOI: 10.7123/01.ASJA.0000417546.66955.6e

being on APT and on that of patients assigned for elective surgery and had stopped their APT for 1 week before surgery.

Patients and methods

The present study was conducted at the Anesthesia Department, Benha University Hospital, from November 2009 to February 2012. After approval of the study protocol and obtaining patient consent, 150 patients undergoing various surgical procedures were enrolled in the study (Table 1). The protocol of this selective study aimed to include 90 patients requiring emergency surgical interference and on APT; these patients were categorized into three equal groups (G1, G2, G3) according to the mode of APT so as to included 30 patients on aspirin alone (ASP group), 30 patients on clopidogrel alone (CLO group), and 30 patients receiving both (combination group); in addition, 30 age-matched and sex-matched patients without any history of APT were enrolled as the control group (G4). The last group (G5) included 30 patients on combined APT and assigned to elective major surgeries who discontinued APT (APT-off) for 7 days before the day of the surgery and were readministered with APT immediately after surgery.

All patients were assessed for preoperative American Society of Anesthesiologists (ASA) score, associated comorbidities, and preoperative hemoglobin (Hb) and platelet counts. The same anesthetic regimen was applied for all study groups; general anesthesia was induced with thiopental (3–5 mg/kg), fentanyl (1–2 μg/kg), and atracurium (0.5 mg/kg), then controlled mask ventilation for 1.5 min was continued with 1.5% isoflurane till complete muscle relaxation. Thereafter, the patient was intubated with an endotracheal tube of suitable size. Anesthesia was maintained using 1% isoflurane and controlled ventilation through a closed circuit system with 100% O_2. Ventilation parameters were a tidal volume of 6–8 ml/kg, a ventilatory rate adjusted to maintain the end tidal CO_2 between 35–40 mmHg, and an inspiratory-to-expiratory ratio (I : E) of 1 : 2.

During the intraoperative period, the following data were recorded: intraoperative complications, operative time, amount of intraoperative blood loss, Hb concentration, and platelet count. Intraoperative transfusion requirements of blood were also recorded, blood was transfused when Hb concentration was less than 8. At the end of surgery, residual neuromuscular block was reversed with neostigmine (0.04 mg/kg) and atropine (0.01 mg/kg), and the patient was extubated when the criteria for extubation were met. After the patient was transferred to the postanesthesia care unit, the following data were recorded during the first 12 h of the postoperative period: blood loss, estimated by the amount of blood collected in the surgical suction drain, Hb concentration and platelet count, and postoperative transfusion requirement of blood. Data on length of hospital stay, need for ICU admission, and length of ICU stay, as well as postoperative morbidity, mortality, and 30-day readmission were recorded.

Statistical analysis

Data were presented as mean ± SD, ranges, numbers, and percentages. Data were obtained using the χ^2-test and one-way analysis of variance for intergroup comparisons. Statistical analysis was carried out using the SPSS for Windows statistical package (version 15, 2006; SPSS Inc., Chicago, Illinois, USA). A P-value less than 0.05 was considered statistically significant.

Results

The study included 150 patients, 86 men (57.3%) and 64 women (42.7%) with a mean age of 59.6 ± 7.3 years; range: 43–78 years. Forty-five patients were ASA grade II, 81 patients were ASA grade III, and 24 patients were ASA grade IV. The mean body weight of enrolled patients was 85.5 ± 8.5 kg; range: 59–98 kg, and the mean height was 167.6 ± 5.8 cm; range: 153–185 cm with a mean BMI of 30.4 ± 3 kg/m^2; range: 19–36 kg/m^2. There was a nonsignificant ($P > 0.05$) difference between studied patients as regards the age, sex, weight, height, BMI, and ASA grade. All patients had comorbidities in varied combinations; however, cardiac lesions are the predominant comorbidity (Table 2).

All patients had a smooth intraoperative course within a mean operative time, which showed a nonsignificant difference between studied groups. All patients who underwent APT showed a significantly greater amount of blood loss both intraoperatively and at 12 h after the end of surgery, with a concomitantly significantly higher number of blood units consumed compared with that in the control group. Emergency patients maintained on clopidogrel showed the least deviation from elective patients who were operated upon while being APT-off. On the contrary, patients included in the combination group showed the worst outcome, manifested as a significantly greater blood loss both intraoperatively and at 12 h postoperatively with a concomitantly significantly higher number of blood units consumed compared with that in

Table 1 Patient distribution according to type of surgical procedure performed

	G1	G2	G3	G4	G5	Total
General surgery	6 (20%)	10 (33.3%)	8 (26.7%)	11 (36.6%)	10 (33.3%)	45 (30%)
Orthopedic	13 (43.3%)	9 (30%)	10 (33.3%)	9 (30%)	10 (33.3%)	51 (34%)
Urology	3 (10%)	4 (13.3%)	2 (6.7%)	4 (13.3%)	2 (6.6%)	15 (10%)
Gynecology	8 (26.6%)	7 (23.7%)	10 (33.3%)	6 (16.7%)	8 (26.6%)	39 (26%)

Data are presented as numbers; percentages are in parentheses.

the CLO group and in the elective APT-off patients. In addition, patients maintained on aspirin showed significantly higher blood loss and a greater need for blood transfusion compared with elective APT-off patients (Table 3, Fig. 1).

All patients showed a significant decrease in the intraoperative Hb concentration compared with their levels estimated preoperatively. However, intraoperative blood transfusion could compensate for the Hb concentration deficit in the control group, which showed a nonsignificant postoperative Hb concentration compared with preoperative concentration, whereas in the other studied groups, postoperative Hb concentration still showed a significant difference compared with preoperative concentration. On the contrary, platelet count showed a nonsignificant difference throughout the course of the study and no patient showed the limiting count for platelet transfusion (Table 3, Fig. 2).

Seven patients required admission to the ICU with a frequency of 4.7%; this included three patients from the elective group, two of whom had ECG abnormalities (ST segment changes) suggestive of ischemic insult, and the third developed acute lung injury and required maintained mechanical ventilation. One patient in the control group had prolonged residual neuromuscular blocking action and was maintained on mechanical ventilation till extubation. The other three patients underwent emergency surgeries. Two of them underwent surgeries for strangulated incisional hernia, which required maintenance on mechanical ventilation because of a continuous drop in arterial oxygen saturation after the reduction of the huge incisional hernia. The third had a fractured pelvis and developed chest pain with ECG abnormalities (an elevated ST segment in the antroseptal leads) with elevated cardiac enzymes suggestive of the development of myocardial infarction. No 30-day readmissions were recorded and no mortality was reported during a mean ICU stay of 2.6 ± 1 days; range: 1–4 days (Table 4, Fig. 3).

The mean total postoperative hospital stay was 18.5 ± 5.1 days; range: 9–31 days. All groups showed a nonsignificant difference as regards the frequency and duration of ICU admission, or the duration of hospital stay (Table 4, Fig. 3).

Discussion

The question to be answered is whether to stop or continue APT before elective surgery especially for patients with appropriate indications for APT use, such as symptomatic carotid disease, recent coronary stents, or recent cardiac insult. The answer is still a matter of controversy.

Through the current study, elective patients who were on combined APT and were APT-off for 1 week showed significantly less blood loss and consumption of blood units compared with those on continued APT due to surgical interference on an emergency basis. Moreover, the difference compared with that in patients who did not previously receive APT was nonsignificant. These data

Table 2 Preoperative data of studied patients

	G1	G2	G3	G4	G5	Total
Age (years)	56.2 ± 5.2 (43–65)	59.6 ± 4.1 (47–65)	62.4 ± 6.4 (45–69)	58.9 ± 7.5 (47–74)	60.6 ± 9 (46–75)	59.6 ± 7.3 (43–78)
M:F	18:12	17:13	16:14	18:12	17:13	86:64
Weight (kg)	83.1 ± 10 (59–95)	85.9 ± 9.2 (59–97)	85.8 ± 7.5 (68–95)	85.4 ± 8.8 (60–94)	85.2 ± 7.3 (68–95)	85.5 ± 8.5 (59–98)
Height (cm)	169.1 ± 7.7 (156–185)	165.8 ± 5 (156–172)	167.5 ± 6.1 (155–178)	167.3 ± 4.4 (158–175)	168.3 ± 4.8 (157–177)	167.6 ± 5.8 (153–185)
BMI (kg/m^2)	29.2 ± 3.9 (18–35.7)	31.2 ± 2.8 (23–36.5)	30.6 ± 2.5 (25–35.7)	30.5 ± 3.1 (23.3–36)	30 ± 2.6 (25.3–35)	30.4 ± 3 (19–36)
ASA grade						
II	9 (30%)	10 (33.3%)	9 (30%)	9 (30%)	8 (26.7%)	45 (30%)
III	18 (60%)	15 (50%)	13 (43.3%)	16 (53.3%)	19 (63.3%)	81 (54)
IV	3 (10%)	5 (16.7%)	8 (26.7%)	5 (16.7%)	3 (10%)	24 (16%)
Associated comorbidities						
Previous AMI	11 (36.7%)	7 (23.3%)	8 (26.7%)	9 (30%)	13 (43.3%)	48 (32%)
Previous CABP	4 (13.3%)	6 (20%)	6 (20%)	5 (16.7%)	4 (13.3%)	25 (16.7%)
Hypertension	10 (33.3%)	9 (30%)	7 (23.3%)	9 (30%)	7 (23.3%)	42 (28%)
DM	7 (23.3%)	8 (26.7%)	6 (20%)	10 (33.4%)	9 (30%)	40 (26.7%)
Previous DVT	3 (10%)	4 (13.3%)	2 (6.6%)	5 (16.7%)	4 (13.3%)	18 (12%)
CRD	1 (3.3%)	2 (6.6%)	1 (3.3%)	3 (10%)	3 (10%)	10 (6.7%)

Data are presented as mean ± SD and numbers; ranges and percentages are in parentheses.
AMI, acute myocardial infarction; ASA, American Society of Anesthesiologists; CABP, coronary artery bypass; CRD, chronic renal disease; DM, diabetes mellitus; DVT, deep vein thrombosis; F, female; M, male.

indicated the fact that limited stoppage of APT could equalize the risk/benefit equation for these patients at risk of thrombotic or bleeding complications.

The choice of discontinuation of APT for 7 days before surgery was dependent on data provided by Collyer *et al.* [10], who sequentially estimated platelet ADP channel inhibition by clopidogrel and found that the mean platelet ADP inhibition was decreased from 71.5 to 67.1% on day 3, 48.8% on day 5, and 36.1% on day 7. Thus, on the seventh day of stoppage, about one-third of the APT activity still prevailed, which could not hamper hemostasis.

Similarly, Ceppa *et al.* [11] reported that patients on clopidogrel can safely undergo major lung resection after discontinuation of clopidogrel for 5 days before surgery and resumption immediately after surgery without differences in rates of perioperative transfusions, reoperations for bleeding, myocardial infarction, and stroke compared with control patients who did not receive perioperative clopidogrel. In addition, Nandi *et al.* [12] found that discontinuation of clopidogrel for at least 5 days before hip or knee arthroplasty may lower the rate of bleeding-related events; no increase in events was observed when patients resumed clopidogrel immediately after surgery.

Moreover, in agreement with the concept of discontinuation of APT for 7 days, Chernoguz *et al.* [13] documented the following data: although clopidogrel use within 7 days of an operation significantly increased the risk of postoperative bleeding, most bleeding episodes were successfully managed by transfusion without an increase in bleeding-related mortality or the necessity for reoperation; high-risk patients undergoing elective operations may not require preoperative clopidogrel cessation, but when clopidogrel cessation is warranted, 7 days before the procedure is recommended. In addition, Oh *et al.* [14] found that the use of APT does not increase the risk of postoperative intraocular bleeding; however, when it is safe to discontinue its use even for a short period of time the potential risk is further reduced.

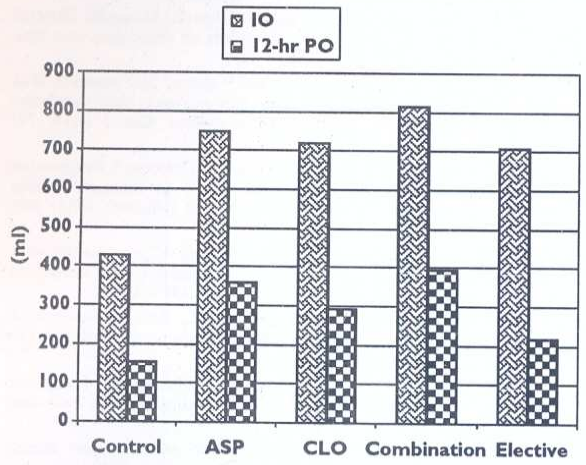
The important applicability for such question must be for emergency surgery where there is no time available for discontinuation. Patients maintained on combination APT showed the worst outcome, manifested as a significantly greater blood loss with a significantly higher need for blood transfusion compared with that in elective APT-off patients and the CLO group. In contrast, patients maintained on clopidogrel showed the least deviation from elective APT-off patients who were operated upon while being APT-off, but still showed a significant difference compared with control patients who were not on APT. In support of these data, Chechik *et al.* [15] found that the mean perioperative blood loss for patients on clopidogrel was significantly more compared with that in patients who are not on clopidogrel but significantly less compared with patients on combined clopidogrel and aspirin. In addition, Taylor *et al.* [16] reported a statistically significant increase in bleeding-associated morbidity in

Table 3 Operative and postoperative data of studied groups

	Control	ASP	CLO	Combination	Elective
Operative time (min)	139.7 ± 34.3 (100–180)	132 ± 26.2 (90–180)	140.2 ± 42.6 (90–225)	137.7 ± 25.1 (100–200)	135.7 ± 25.1 (100–200)
Blood loss (ml)					
IO	428.3 ± 120 (150–750)	747.3 ± 192[b] (450–1200)	717.3 ± 155[b,d] (400–1100)	814 ± 174[b] (560–1150)	707.3 ± 155[b,c,d] (350–1000)
12-h PO	154.7 ± 70.9 (100–350)	357 ± 140[b] (200–700)	291.7 ± 158.9[b,d] (100–650)	393.3 ± 226[b] (200–850)	217.2 ± 120[b,d] (100–450)
Number of transfused blood units	1.5 ± 0.6 (1–3)	2.7 ± 0.8[b] (1–4)	2.4 ± 0.7[b] (1–3)	2.9 ± 0.9[b] (2–4)	2.1 ± 0.7[b,c,d] (1–3)
Hemoglobin concentration					
Pre	11 ± 0.5 (9.8–11.6)	11.2 ± 0.9 (9.5–11.9)	11.4 ± 0.4 (10.2–11.9)	11.2 ± 0.6 (9.2–11.7)	11.1 ± 0.7 (9.3–12)
IO	10.6 ± 0.7[a] (8.3–11.3)	10.2 ± 1.1[a] (8.5–11.2)	10.2 ± 1[a] (8.8–11.3)	9.8 ± 1.1[a] (8.7–11.1)	10.4 ± 0.7[a] (8.2–11.3)
PO	10.8 ± 0.5 (9.4–11.6)	10 ± 0.8[a] (8.7–11)	10.1 ± 0.9[a] (9–11.2)	10 ± 0.8[a] (8.7–11.2)	10.6 ± 0.7[a] (9–11.6)
Platelet count (10^3 platelets/ml)					
Pre	195.3 ± 29 (123–235)	190.1 ± 33.1 (136–247)	189.9 ± 38.2 (123–246)	186.3 ± 39.9 (110–247)	202.8 ± 29 (133–231)
IO	185.6 ± 27.6 (116–223)	177.8 ± 31 (128–231)	176.6 ± 35.6 (114–229)	172.3 ± 36.9 (100–228)	190.1 ± 27.2 (125–217)
PO	186.5 ± 27.7 (117–224)	180.6 ± 31.4 (130–235)	179.4 ± 36.1 (116–232)	175 ± 37.5 (103–232)	193.7 ± 27.6 (127–220)

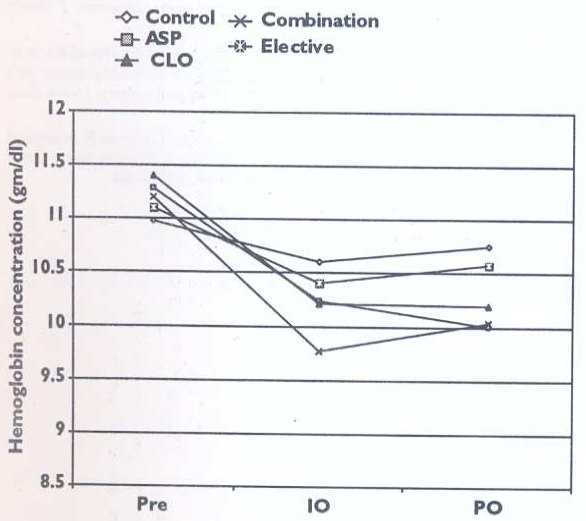
Data are presented as mean ± SD and numbers; ranges and percentages are in parentheses.
ASP, aspirin; CLO, clopidogrel; IO, intraoperative; PO, postoperative; pre, postoperative.
[a]Significant versus preoperative.
[b]Significant versus control group.
[c]Significant versus ASP group.
[d]Significant versus combination group.
[e]Significant versus CLO group.

Figure 1



Mean blood loss recorded in studied groups.

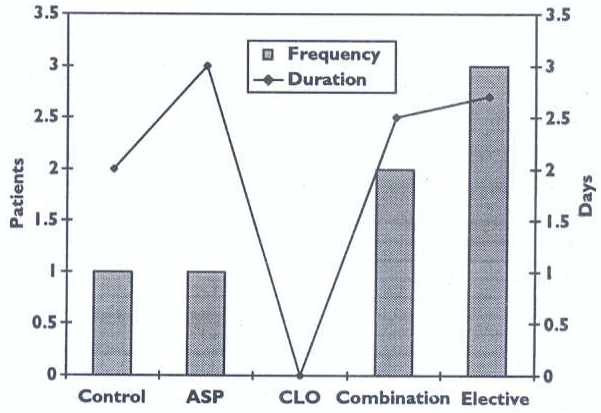
Figure 2



Mean hemoglobin concentration estimated throughout the study period in studied groups.

patients who continued their APT or anticoagulant therapy and in those who discontinued therapy perioperatively compared with the controls not prescribed with any antiplatelet or anticoagulant drugs and concluded that patients on APT or anticoagulant therapy have a higher rate of perioperative bleeding compared with those who are not on APT.

Figure 3



Postoperative intensive care unit data of studied groups.

Analysis of results obtained on patients maintained on clopidogrel alone indicated that continuation on chronic clopidogrel therapy was not associated with a high risk of bleeding compared with that in patients who stopped APT for 1 week before elective surgery and points to its safety in comparison with aspirin administered alone or in combination. Commensurate with the safety of continuation of clopidogrel therapy, Christy *et al.* [17] reported that preinjury use of APT does not independently affect morbidity or mortality in trauma patients with pelvic fixation, but is associated with an increased likelihood of receiving packed red blood cell transfusions within 24 h of admission, and only preinjury aspirin versus clopidogrel or nonsteroidal anti-inflammatory drugs was associated with early packed red blood cell transfusions. Stone *et al.* [18] reported that patients undergoing peripheral arterial surgery in whom clopidogrel was continued either alone or as part of dual APT did not have significant bleeding complications compared with patients who were not on APT or were on ASA alone at the time of surgery, and concluded that clopidogrel can safely be continued. Chechik *et al.* [19] found that early surgical intervention for hip fracture in patients receiving long-term treatment with clopidogrel appears to be safe in terms of bleeding complications and has the potential to enable earlier mobilization and shorter hospitalization and may reduce mortality and complications associated with immobilization.

Table 4 Postoperative data

	Control	ASP	CLO	Combination	Elective	Total
ICU data						
Frequency	1 (3.3%)	1 (3.3%)	0	2	3	7
Duration (days)	2	3	0	2.5 ± 0.7 (2–3)	2.7 ± 1.5 (1–4)	2.6 ± 1 (1–4)
Duration of hospital stay (days)	17.8 ± 4.9 (9–27)	18.7 ± 5.2 (10–30)	18.8 ± 5.7 (9–25)	18.3 ± 4.6 (11–27)	18.9 ± 5.3 (10–31)	18.5 ± 5.1 (9–31)

Data are presented as numbers and mean ± SD; percentages and ranges are in parentheses.
ASP, aspirin; CLO, clopidogrel; IO, intraoperative; PO, postoperative; pre, postoperative.

Conclusion

The obtained results and review of the literature allowed us to conclude that for elective surgery stoppage of APT for 7 days, if not hazardous, is advisable. Emergency surgical procedures for patients maintained on chronic APT are not so harmful despite the increased need for transfusions; however, the outcome is best in those receiving clopidogrel alone.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

References

1 Gauchet C. ADP receptors of platelets and their inhibition. Thromb Haemost 2001; 86:222–232.

2 Diener HC, Bogousslavsky J, Brass LM, Cimminiello C, Csiba L, Kaste M, *et al.* MATCH investigators. Aspirin and clopidogrel compared with clopidogrel alone after recent ischaemic stroke or transient ischaemic attack in high-risk patients (MATCH): randomized, double-blind, placebo-controlled trial. Lancet 2004; 364:331–337.

3 Yokoi H, Kimura T, Isshiki T, Ogawa H, Ikeda Y. Pharmacodynamic assessment of a novel P2Y(12) receptor antagonist in Japanese patients with coronary artery disease undergoing elective percutaneous coronary intervention. Thromb Res 2012; 129:623–628.

4 Orford JL, Fasseas P, Melby S, Burger K, Steinhubl SR, Holmes DR, Berger PB. Safety and efficacy of aspirin, clopidogrel, and warfarin after coronary stent placement in patients with an indication for anticoagulation. Am Heart J 2004; 147:463–467.

5 Haydar AA, Abchee AB, El-Hajj II, Hujairi NM, Tfaili AS, Hatoum T, *et al.* Bleeding post coronary artery bypass surgery. Clopidogrel – cure or culprit? J Med Liban 2006; 54:11–16.

6 Kang W, Theman TE, Reed JF III, Stoltzfus J, Weger N. The effect of preoperative clopidogrel on bleeding after coronary artery bypass surgery. J Surg Educ 2007; 64:88–92.

7 Oates-Whitehead RM, D'Angelo A, Mol B. Withdrawn: anticoagulant and aspirin prophylaxis for preventing thromboembolism after major gynaecological surgery. Cochrane Database Syst Rev 2003; 4:CD003679.

8 Fleming MD, Stone WM, Scott P, Chapital AB, Fowl RJ, Money SR. Safety of carotid endarterectomy in patients concurrently on clopidogrel. Ann Vasc Surg 2009; 23:612–615.

9 Mariscalco G, Bruno VD, Cottini M, Borsani P, Banach M, Piffaretti G, *et al.* Optimal timing of discontinuation of clopidogrel and risk of blood transfusion after coronary surgery. Propensity score analysis. Circ J 2011; 75: 2805–2812.

10 Collyer TC, Reynolds HC, Truyens E, Kilshaw L, Corcoran T. Perioperative management of clopidogrel therapy: the effects on in-hospital cardiac morbidity in older patients with hip fractures. Br J Anaesth 2011; 107: 911–915.

11 Ceppa DP, Welsby IJ, Wang TY, Onaitis MW, Tong BC, Harpole DH, *et al.* Perioperative management of patients on clopidogrel (Plavix) undergoing major lung resection. Ann Thorac Surg 2011; 92:1971–1976.

12 Nandi S, Aghazadeh M, Talmo C, Robbins C, Bono J. Perioperative clopidogrel and postoperative events after hip and knee arthroplasties. Clin Orthop Relat Res 2012; 479:1436–1441.

13 Chernoguz A, Telem DA, Chu E, Ozao-Choy J, Tammaro Y, Divino CM. Cessation of clopidogrel before major abdominal procedures. Arch Surg 2011; 146:334–339.

14 Oh J, Smiddy WE, Kim SS. Antiplatelet and anticoagulation therapy in vitreoretinal surgery. Am J Ophthalmol 2011; 151:934–939.

15 Chechik O, Thein R, Fichman G, Haim A, Tov TB, Steinberg EL. The effect of clopidogrel and aspirin on blood loss in hip fracture surgery. Injury 2011; 42:1277–1282.

16 Taylor K, Filgate R, Guo DY, Macneil F. A retrospective study to assess the morbidity associated with transurethral prostatectomy in patients on antiplatelet or anticoagulant drugs. BJU Int 2011; 108 (Suppl 2): 45–50.

17 Christy JM, Stawicki SP, Jarvis AM, Evans DC, Gerlach AT, Lindsey DE, *et al.* The impact of antiplatelet therapy on pelvic fracture outcomes. J Emerg Trauma Shock 2011; 4:64–69.

18 Stone DH, Goodney PP, Schanzer A, Nolan BW, Adams JE, Powell RJ, *et al.* Vascular Study Group of New England. Clopidogrel is not associated with major bleeding complications during peripheral arterial surgery. J Vasc Surg 2011; 54:779–784.

19 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; 29:63–68.