Safety of the cardiac triple therapy: The experience of the Quebec Heart Institute

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BACKGROUND: Contemporary treatment of acute coronary syndrome is based on the combination of acetylsalicylic acid (ASA) and clopidogrel. However, an increasing proportion of patients with cardiovascular disease also have an indication for anticoagulant therapy with warfarin. The combination of ASA, clopidogrel and warfarin, also called the cardiac triple therapy (CTT), is emerging in clinical practice, although little is known about its safety.

OBJECTIVES: To determine the risk of major and minor bleeding associated with the CTT compared with two other regimens using the combination of either ASA and clopidogrel or ASA and warfarin in patients with cardiovascular disease.

METHODS: A retrospective study was performed of all susceptible patients who may have received the CTT on discharge from the Quebec Heart Institute (Sainte-Foy, Quebec) between 2002 and 2005. The charts of patients treated with the CTT, ASA and clopidogrel, or ASA and warfarin were reviewed and patients were interviewed to document any bleeding episodes.

RESULTS: A total of 183 patients were studied. Overall bleeding in the CTT group was 3% compared with 5% in the group receiving ASA and clopidogrel and 16% in the group receiving ASA and warfarin ($P=0.03$). Patients who experienced bleeding were older, had more hypertension and had been exposed to their drug regimens for a longer duration. There was no significant difference in major bleeding episodes.

CONCLUSIONS: The CCT appears to be relatively safe compared with other regimens. Higher bleeding rates within the ASA-warfarin group emphasize the need to carefully educate and follow patients on combination therapy.

Key Words: Acetylsalicylic acid; Anticoagulants; Bleeding; Clopidogrel; Warfarin

Within the past few years, the antithrombotic treatment of acute coronary syndrome (ACS) has evolved greatly. The combination of acetylsalicylic acid (ASA) and thienopyridines has been proven in randomized clinical trials to be superior to a regimen of ASA and warfarin in patients undergoing coronary stent implantation (1-4). Its benefits were seen as fewer adverse cardiac events and a reduced rate of hemorrhagic complications. More recently, long-term, dual antiplatelet therapy using ASA and clopidogrel has shown advantages in managing patients with ACS, whether in association with percutaneous coronary intervention (PCI) or not (5-8). This has evolved into the current guidelines for the antithrombotic treatment of patients with ACS (9-11). However, in contemporary clinical practice, cardiologists are faced with an aging population with more comorbidities. Also, many patients suffering from ACS are

Sécurité de la triple thérapie cardiaque : L'expérience de l'Institut de Cardiologie de Québec

INTRODUCTION: Le traitement moderne du syndrome coronarien aigu (SCA) est maintenant basé sur l'utilisation de la combinaison d'aspirine et de clopidogrel. Une proportion importante de patients avec maladie cardiovasculaire a également une indication d'anticoagulation. La triple thérapie cardiaque (TTC) émerge comme une nouvelle approche dans l'arsenal de traitements de tel patient malgré que peu de données existent sur sa sécurité.

OBJECTIF: Déterminer le risque de saignement majeur et mineur associé à la TTC comparé à la combinaison d'Aspirine-Clopidogrel et la combinaison d'Aspirine-Warfarine chez des patients avec maladie cardiovasculaire.

MÉTHODES: Étude rétrospective de tous les patients susceptibles d'avoir été libérés de notre institution avec la triple thérapie cardiaque entre 2002 et 2005. Les patients avec un traitement correspondant à un des trois groupes parmi la TTC, Aspirine et Clopidogrel ou Aspirine et Warfarine, voyaient leurs dossiers révisés et étaient soumis à un questionnaire téléphonique pour identifier tout épisode de saignement.

RÉSULTATS: Cent quatre-vingt-trois patients ont été inclus. Le taux de saignement global dans chacun des groupes était pour la TTC de 3%, pour le groupe Aspirine-Clopidogrel 5% et, pour le groupe Aspirine-Warfarine 16%. En comparant les 3 groupes, cette différence était statistiquement significative ($p=0.03$), mais il n'y avait pas de différence significative pour les saignements majeurs.

CONCLUSIONS: L'utilisation de la triple thérapie cardiaque apparaît sécuritaire comparé aux régimes thérapeutiques standards. Un taux de saignement plus élevé dans le groupe aspirine-warfarine met l'accent sur le besoin de suivre de près les patients sous warfarine.

already receiving chronic anticoagulation with warfarin. Indeed, atrial fibrillation (AF), mechanical cardiac valves, very low left ventricle ejection fraction and thromboembolic disorders are medical conditions that may also benefit from the association of antiplatelet therapy and anticoagulation. This cardiac triple therapy (CTT) – ASA, clopidogrel and warfarin – may be needed in these patients and is now often encountered in daily practice. Evidence-based medicine about the safety of such a regimen is sparse and there are concerns about the bleeding risk. Many studies (12-16) have yielded contradictory results regarding the bleeding risks of the CTT, adding to the confusion over which strategy should be adopted. From this lack of evidence have emerged many empirical treatment regimens that physicians can apply to similar clinical problems (17,18). Accordingly, various approaches have been developed to avoid

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using the CTT or to reduce the duration of treatment. For example, some patients may receive a bare-metal stent instead of a drug-eluting stent to shorten the duration of thienopyridine therapy (19,20), and other patients with AF and low thromboembolic risk may be encouraged to cease their warfarin use while on dual antiplatelet therapy (21). All of these strategies are targeted at reducing a potential increase in bleeding risk with the CTT. Therefore, the aim of the present study was to assess bleeding risk of the CTT compared with two other frequently used drug regimens comprising the combination of either ASA and clopidogrel or ASA and warfarin.

METHODS

A retrospective review of the charts of all susceptible patients who may have received the CTT at the Quebec Heart Institute (Sainte-Foy, Quebec) between 2002 and 2005 was performed. Using file research criteria, any adult patients hospitalized with a diagnosis of ACS, AF or mechanical valve replacement were identified. From these criteria, patient charts were then screened to identify patients who were discharged from the institution with one of the following three treatment regimens: ASA and clopidogrel (A+C); ASA and warfarin (A+W); or ASA, clopidogrel and warfarin (CTT). These patients may or may not have undergone PCI.

Clinical end points evaluated after patient discharge were major bleeding and minor bleeding, according to definitions published in large studies (5,6). Major bleeding was defined as bleeding with any of the following characteristics: fatal; disabling; intracranial; intraocular, associated with loss of vision; associated with a hemoglobin decrease of 50 g/L or greater; requiring a surgical intervention or positive inotropes; or requiring two or more blood transfusions. Minor bleeding was defined as any other bleeding complications requiring discontinuation of the medication. Demographic characteristics and bleeding events were collected from patient charts. Patients were also contacted by phone using a comprehensive questionnaire to identify or confirm bleeding. Consent was obtained to contact their pharmacist, who was called to confirm the drug regimen and to correctly record the starting and ending date of medication. Hospital records from other institutions were obtained after patient consent and were carefully reviewed for any episodes of major bleeding when applicable. Patients were excluded from the study if they could not be contacted or if their drug regimen could not be confirmed by the pharmacist. The study was performed with the approval of the hospital ethics committee. Written consent was obtained for all patients.

Statistical analysis

Patients were classified into three groups according to their treatment at discharge. Group 1 comprised patients receiving A+W, group 2 received A+C and group 3 received the CTT. Results are expressed as mean $\pm$ SD or percentages unless otherwise specified. The three groups were compared for statistical significance using one-way analysis of variance, χ^2 test and Fischer's exact test as appropriate. The statistical comparison between patients with bleeding versus those with no bleeding was performed using a Student's *t* test, χ^2 test and Fischer's exact test as appropriate. $P < 0.05$ was considered significant.

RESULTS

Four hundred sixty patient charts were identified for review by file research criteria. A total of 183 patients were included in the study: 79 patients received the CTT, 59 received A+C and

TABLE 1
Clinical characteristics of patients with respect to therapy

Baseline characteristics	Total cohort (n=183)	Group 1, A+W (n=45)	Group 2, A+C (n=59)	Group 3, CTT (n=79)	P
Male sex	128 (70)	30 (67)	41 (69)	57 (72)	NS
Age, years (mean $\pm$ SD)	70.7 $\pm$ 11	73 $\pm$ 1	69 $\pm$ 1	71 $\pm$ 1	NS
Hypertension	107 (58)	33 (73)	29 (49)	45 (57)	0.04
LVEF $\leq$ 30%	30 (16)	4 (9)	2 (3)	24 (30)	<0.0001
Follow-up, days (mean $\pm$ SD)	346 $\pm$ 403	653 $\pm$ 444	366 $\pm$ 366	156 $\pm$ 278	<0.0001
Congestive heart failure	58 (32)	11 (24)	17 (29)	30 (38)	NS
Coronary angiography	146 (80)	9 (20)	59 (100)	78 (99)	<0.0001
Radial access	132 (90)	8 (89)	54 (92)	70 (90)	NS
Femoral access	14 (10)	1 (11)	5 (8)	8 (10)	NS
PCI with bare-metal stent	136 (74)	7 (78)	57 (97)	72 (91)	NS
PCI with DES	7 (4)	0 (0)	1 (2)	6 (8)	NS
ASA dosage					
$\leq$ 81 mg	171 (93)	42 (93)	53 (90)	76 (96)	NS
160 mg	1 (0.5)	1 (2)	0 (0)	0 (0)	NA
325 mg	11 (6)	2 (4)	6 (10)	3 (4)	NA
Proton pump inhibitor	84 (46)	20 (44)	26 (44)	38 (48)	NS

All values are given as n (%) unless otherwise indicated. A+W Acetylsalicylic acid (ASA) and warfarin; A+C ASA and clopidogrel; CTT Cardiac triple therapy consisting of ASA, clopidogrel and warfarin; DES Drug-eluting stent; LVEF Left ventricular ejection fraction; PCI Percutaneous coronary intervention

45 patients received A+W. Two hundred seventy-seven patients were excluded from the analysis. The two main reasons for exclusion were inability to be reached by phone and drug regimen not fitting one of the groups when verified by the pharmacist.

Baseline characteristics of all three groups are shown in Table 1. The groups were similar with few exceptions. The CTT group included more patients with left ventricular ejection fraction less than 30% and who received the drug regimen for a shorter period of time. The A+W group had more patients with hypertension. As expected, the CTT and A+C groups had a larger proportion of patients who had undergone coronary angiography. There was no difference among the three groups in prevalence of coronary artery disease, major risk factors (hypertension, diabetes mellitus, hypercholesterolemia and smoking), stroke, chronic renal failure or the presence of valve prostheses. Medical treatment (beta-blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, statins and diuretics) was otherwise similar among the groups.

Table 2 shows the baseline characteristics of patients with and without bleeding. Patients who bled were older, had more hypertension and had been exposed to their respective regimen for a longer duration. For all other variables, there were no differences between patients with or without bleeding. Proton pump inhibitor (pantoprazole, omeprazole, esomeprazole, rabeprazole and lansoprazole) use was observed in 46% of the entire cohort with similar rates between patients with and without bleeding.

During a mean follow-up of 346 $\pm$ 403 days, only 12 patients (7%) experienced significant bleeding (Table 3). Of those, seven patients (16%) were in the A+W group, three patients (5%) were in the A+C group and two patients (3%) were receiving the CTT ($P=0.03$). Minor bleeding occurred in the A+W and A+C groups but none occurred in the CTT group. No difference was observed for major bleeding among the

TABLE 2
Baseline characteristics of patients with respect to bleeding events

Baseline characteristics	Total cohort (n=183)	Patients with bleeding (n=12)	Patients without bleeding (n=171)	P
Male sex	128 (70)	9 (75)	119 (70)	NS
Age, years (mean ± SD)	70.7±11	76±10	70±9	0.01
Known CAD	151 (83)	11 (92)	140 (82)	NS
Resuscitated sudden death	10 (5)	0 (0)	10 (6)	NS
Hypertension	107 (58)	10 (83)	97 (57)	0.06
Hypercholesterolemia	109 (60)	6 (50)	103 (60)	NS
Active smoking	21 (11)	2 (17)	19 (11)	NS
Diabetes	48 (26)	3 (25)	45 (26)	NS
LVEF (mean ± SD)	46±16	50±15	45±16	NS
LVEF ≤30%	30 (16)	3 (25)	27 (16)	NS
Mean follow-up*, days	346±403	594±489	329±392	0.03
Ischemic stroke	16 (9)	2 (17)	14 (8)	NS
Hemorrhagic stroke	1 (0.5)	0 (0)	1 (0.6)	NA
Congestive heart failure	58 (32)	4 (33)	54 (32)	NS
Chronic renal failure	34 (19)	4 (33)	30 (18)	NS
Mechanical cardiac valve	5 (3)	0 (0)	5 (3)	NS
PCI with stent	136 (74)	7 (58)	129 (75)	NS
PCI with DES	7 (4)	0 (0)	7 (4)	NS
Radial access	132 (72)	6 (50)	126 (74)	NS
Femoral access	14 (8)	1 (8)	13 (8)	NS
ASA dosage				
≤81 mg	171 (93)	10 (83)	161 (94)	NS
160 mg	1 (0.5)	0 (0)	1 (0.6)	NS
325 mg	11 (6)	2 (17)	9 (5)	NS
Proton pump inhibitors	84 (46)	7 (58)	77 (45)	NS
ACEIs	100 (55)	5 (42)	95 (56)	NS
ARBs	38 (21)	2 (17)	36 (21)	NS
Calcium channel blockers	52 (28)	3 (25)	49 (29)	NS
Beta-blockers	138 (75)	11 (92)	127 (74)	NS

All values are given as n (%) unless otherwise indicated. *Follow-up is defined as the duration of treatment for a specific drug regimen. ACEI Angiotensin-converting enzyme inhibitors; ARBs Angiotensin receptor blockers; ASA Acetylsalicylic acid; CAD Coronary artery disease; DES Drug-eluting stent; LVEF Left ventricular ejection fraction; NS Not significant; PCI Percutaneous coronary intervention

three groups – three patients (7%) in the A+W group, one patient (2%) in the A+C group and two patients (3%) in the CTT group experienced a serious and/or life-threatening bleeding event ($P=0.4$). Among patients with major bleeding, the international normalized ratio (INR) at the time of event was reviewed. An INR value above the therapeutic range was observed in two of three major bleeding episodes in the A+W group, and in one of two major episodes in the CTT group.

DISCUSSION

To our knowledge, this is only the second study comparing the safety of the CTT with that of dual antiplatelet therapy for a period longer than 30 days (14). However, we were the first to add a third treatment group receiving A+W for direct comparison. This retrospective observational study, among a few others (12-16), was undertaken to assess the bleeding risk associated with the CTT. Previous studies have yielded controversial results regarding the risk of bleeding with this course of therapy. Some have found higher risk of bleeding (12,14-16),

TABLE 3
Bleeding events in the three treatment groups

Variables	Total cohort (n=183)	Group 1, A+W (n=45)	Group 2, A+C (n=59)	Group 3, CTT (n=79)	P
Overall bleeding, n (%)	12 (7)	7 (16)	3 (5)	2 (3)	0.03
Minor bleeding, n (%)	6 (3)	4 (9)	2 (3)	0 (0)	0.015
Major bleeding, n (%)	6 (3)	3 (7)	1 (2)	2 (3)	NS

A+W Acetylsalicylic acid (ASA) and warfarin; A+C ASA and clopidogrel; CTT Cardiac triple therapy consisting of ASA, clopidogrel and warfarin; NS Not significant

while others did not observe a risk increment (13).

Our results indicate a very low incidence of bleeding among the three groups studied. Only six (3%) major and six (3%) minor bleeding events were documented in the total cohort within a mean follow-up of nearly one year. There was a trend toward a higher incidence of major bleeding in the A+W group. This observation was also noted in other studies and could be related to the intensity of treatment with warfarin (9,22). Indeed, 66% of patients with major bleeding in the A+W group and 50% in the CTT group had INR values well above the therapeutic range. Our findings regarding the safety of the CTT are reassuring. The overall bleeding incidence of 3% observed in this study is lower than that in other studies involving the CTT, in which bleeding was encountered in 9.2% to 21.5% of patients (13-15).

To explain the very low incidence of events with the CTT in our study, the possibility of a selection bias must be considered. Patients exposed to the CTT may have been carefully selected by the physicians because of fear of potentially excessive bleeding. Indeed, patients with a bleeding history, non-compliant patients, or those without tight follow-up by their pharmacist and general practitioner may not have been considered for the CTT. Moreover, the CTT may have led physicians to pursue a careful follow-up of these patients. In contrast, the routinely used combination of ASA+W may have called for less attention and may have been used with less supervision than the CTT. The low bleeding incidence may also be explained by the time frame used in the present study, which only considered patients after discharge. Indeed, patients who already had subclinical lesions predisposing to bleeding (ie, gastric erosion or neoplastic colon lesion) may not have tolerated clopidogrel loading and the use of glycoprotein IIb/IIIa antagonists such that patients may have experienced bleeding episodes close to the time of the PCI procedure and/or before discharge from the hospital. More importantly, PCI access site bleeding accounted for a large proportion of the bleeding reported in previous studies (3,4,13,15). At the Quebec Heart Institute, greater than 90% of PCIs are performed using a radial access, resulting in less access site bleeding (23). Also, the high use of proton pump inhibitors in the entire cohort may also have reduced the incidence of bleeding in the present study.

The low bleeding incidence observed in the present study causes us to believe that if, in a selected population, the CTT is thought to be the best therapeutic option for a given patient, it is reasonable to use it. Nevertheless, a careful monitoring of the INR should be instituted and maintained for the duration of treatment. Proton pump inhibitors should also be considered among those patients.

Our results strongly support that when clinically indicated, dual antiplatelet therapy may be prescribed with anticoagulation (CTT) without expecting a higher incidence of bleeding than

with ASA+W. This was shown for patients who had been taking the CTT for a mean follow-up of approximately five months. These observations provide more information on a frequent clinical question about how long a patient can safely remain on clopidogrel while receiving ASA+W. The focus should be on the shorter time of exposure to drugs while on the CTT than while on the other drug regimens. In the era of drug-eluting stents, with recent concerns about late thrombosis and the issue of optimal timing for clopidogrel discontinuation, our observation may somehow reassure clinicians about the CTT. Obviously, more work is needed to document the safety of long-term triple therapy; it is obvious that a prospective clinical trial must be performed.

Limitations

In the present observational study, patients were contacted by phone to document bleeding. Some biases, such as recall bias, may have influenced this assessment, resulting in an underestimation or overestimation of bleeding events. More importantly, a selection bias may have resulted in the CTT being prescribed for patients with a lower bleeding risk. Moreover, we excluded patients for whom it was impossible to ascertain data, thus eliminating deceased patients, some of whom may have died from major bleeding.

CONCLUSION

In the present study, a relatively low bleeding incidence of 3% was found in patients receiving the CTT. Moreover, the bleeding rate with the CTT was not higher than that with other regimens frequently used. Considering that patients with ACS with an indication for anticoagulation represent approximately 5% of patients undergoing revascularization (24), this gives further insight to clinicians considering the CTT as the most appropriate management strategy to prevent thrombotic events. The highest bleeding risk was observed in the ASA+W group, in which two-thirds of major bleeding events were associated with out-of-range therapeutic INR values. This fact emphasizes the importance of careful monitoring for patients requiring anticoagulant therapy.

REFERENCES

- Schomig A, Neumann FJ, Kastrati A, et al. A randomized comparison of antiplatelet and anticoagulant therapy after the placement of coronary-artery stents. *N Engl J Med* 1996;334:1084-9.
- Leon MB, Baim DS, Popma JJ, et al. A clinical trial comparing three antithrombotic-drug regimens after coronary-artery stenting. Stent Anticoagulation Restenosis Study Investigators. *N Engl J Med* 1998;339:1665-71.
- Bertrand ME, Legrand V, Boland J, et al. Randomized multicenter comparison of conventional anticoagulation versus antiplatelet therapy in unplanned and elective coronary stenting. The full anticoagulation versus aspirin and ticlopidine (fantastic) study. *Circulation* 1998;98:1597-603.
- Urban P, Macaya C, Rupprecht HJ, et al. Randomized evaluation of anticoagulation versus antiplatelet therapy after coronary stent implantation in high-risk patients: The multicenter aspirin and ticlopidine trial after intracoronary stenting (MATTIS). *Circulation* 1998;98:2126-32.
- 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. (Errata in 2001;345:1716 and 2001;345:1506).
- Mehta SR, Yusuf S, Peters RJ, et al; Clopidogrel in Unstable angina to Prevent Recurrent Events trial (CURE) Investigators. Effects of pretreatment with clopidogrel and aspirin followed by long-term therapy in patients undergoing percutaneous coronary intervention: The PCI-CURE study. *Lancet* 2001;358:527-33.
- Sabatine MS, Cannon CP, Gibson CM, et al; CLARITY-TIMI 28 Investigators. Addition of clopidogrel to aspirin and fibrinolytic therapy for myocardial infarction with ST-segment elevation. *N Engl J Med* 2005;352:1179-89.
- Steinhuyl SR, Berger PB, Mann JT, et al; CREDO Investigators. Clopidogrel for the Reduction of Events During Observation. Early and sustained dual oral antiplatelet therapy following percutaneous coronary intervention: A randomized controlled trial. *JAMA* 2002;288:2411-20. (Erratum in 2003;289:987)
- Popma JJ, Berger P, Ohman EM, Harrington RA, Grines C, Weitz JL. Antithrombotic therapy during percutaneous coronary intervention: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest* 2004;126(3 Suppl):576S-599S.
- Silber S, Albertsson P, Aviles FF, et al; European Society of Cardiology. [Percutaneous coronary interventions. Guidelines of the European Society of Cardiology-ESC.] *Kardiol Pol* 2005;63:265-320; discussion 321-3.
- Braunwald E, Antman EM, Beasley JW, et al; American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients With Unstable Angina). ACC/AHA guideline update for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction – 2002: Summary article: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients With Unstable Angina). *Circulation* 2002;106:1893-900.
- Buresly K, Eisenberg MJ, Zhang X, Pilote L. Bleeding complications associated with combinations of aspirin, thienopyridine derivatives, and warfarin in elderly patients following acute myocardial infarction. *Arch Intern Med* 2005;165:784-9.
- Porter A, Konstantino Y, Iakobishvili Z, Shachar L, Battler A, Hasdai D. Short-term triple therapy with aspirin, warfarin, and a thienopyridine among patients undergoing percutaneous coronary intervention. *Catheter Cardiovasc Interv* 2006;68:56-61.
- Khurram Z, Chou E, Minutello R, et al. Combination therapy with aspirin, clopidogrel and warfarin following coronary stenting is associated with a significant risk of bleeding. *J Invasive Cardiol* 2006;18:162-4.
- Orford JL, Fasseas P, Melby S, et al. Safety and efficacy of aspirin, clopidogrel, and warfarin after coronary stent placement in patients with an indication for anticoagulation. *Am Heart J* 2004;147:463-7.
- Konstantino Y, Iakobishvili Z, Porter A, et al. Aspirin, warfarin and a thienopyridine for acute coronary syndromes. *Cardiology* 2006;105:80-5.
- Lip GY, Karpha M. Anticoagulant and antiplatelet therapy use in patients with atrial fibrillation undergoing percutaneous coronary intervention: The need for consensus and a management guideline. *Chest* 2006;130:1823-7.
- Rubboli A, Colletta M, Sangiorgio P, Di Pasquale G. Antithrombotic strategies in patients with an indication for long-term anticoagulation undergoing coronary artery stenting: Safety and efficacy data from a single center. *Ital Heart J* 2004;5:919-25.
- Levine GN, Kern MJ, Berger PB, et al; American Heart Association Diagnostic and Interventional Catheterization Committee and Council on Clinical Cardiology. Management of patients undergoing percutaneous coronary revascularization. *Ann Intern Med* 2003;139:123-36.
- Berger PB, Bell MR, Hasdai D, Grill DE, Melby S, Holmes DR Jr. Safety and efficacy of ticlopidine for only 2 weeks after successful intracoronary stent placement. *Circulation* 1999;99:248-53.
- Lorenzoni R, Lazzerini G, Cocci F, De Caterina R. Short-term prevention of thromboembolic complications in patients with atrial fibrillation with aspirin plus clopidogrel: The Clopidogrel-Aspirin Atrial Fibrillation (CLAAF) pilot study. *Am Heart J* 2004;148:e6.
- Landefeld CS, Rosenblatt MW, Goldman L. Bleeding in outpatients treated with warfarin: Relation to the prothrombin time and important remediable lesions. *Am J Med* 1989;87:153-9.
- Bertrand OF, De Larochelliere R, Rodes-Cabau J, et al; Early Discharge After Transradial Stenting of Coronary Arteries Study Investigators. A randomized study comparing same-day home discharge and abciximab bolus only to overnight hospitalization and abciximab bolus and infusion after transradial coronary stent implantation. *Circulation* 2006;114:2636-43.
- Helft G, Gilard M, Le Feuvre C, Zaman AG. Drug insight: Antithrombotic therapy after percutaneous coronary intervention in patients with an indication for anticoagulation. *Nat Clin Pract Cardiovasc Med* 2006;3:673-80.