AHC Media

Clinical Cardiology [ALERT]

Critical analysis of the latest clinical research in cardiovascular medicine

Vol. 33, Issue 10, October 2014
www.ahcmedia.com

ABSTRACT & COMMENTARY

Peri-procedural Management of New Oral Anticoagulants

By Michael H. Crawford, MD, Editor

SOURCE: Beyer-Westendorf J, et al. Peri-interventional management of novel oral anticoagulants in daily care: Results from the prospective Dresden NOAC registry. *Eur Heart J* 2014;35:1888-1896.

Due to the short half-life and rapid onset of action of the new oral anticoagulants (NOACs), peri-procedural anticoagulant free time intervals should be shorter than with warfarin. Thus, there is uncertainty about the use of heparin bridging. These investigators from Germany analyzed the Dresden NOAC registry data to assess peri-procedural NOAC management and safety until 30 days post-procedure. The primary effectiveness outcome was a combination of centrally adjudicated cardiovascular events, including death. The primary safety outcome was the rate of major bleeding events. Among the 2179 patients, 27% underwent procedures (16% minimal, 74% minor, and 10% major). Most of the patients were on rivaroxaban (76%) for stroke prevention in atrial fibrillation (81%). Peri-procedure, 1% of these patients had a major cardiovascular event and 1.2% had major bleeding. The rates of these complications were highest for major procedures (5% and 8%, respectively). During the 863 procedures, NOACs were continued in 22%, temporarily stopped in 49%, or stopped with heparin bridging in 29%. The median time of NOAC interruption was 3 days (2 days before and 1 day after the procedure). Major cardiovascular event rates were similar for those with and without heparin bridging (1.6% vs 0.8%, P = NS), but major bleeding complications were higher with heparin bridging (2.27% vs 0.5%, $P = 0.01$). However, on multivariate analysis, major procedures were independently associated with major bleeding (odds ratio [OR], 16.8; $P < 0.001$), but heparin bridging, which was more commonly used with major procedures, was not. The authors concluded that continuation or brief interruptions in NOAC therapy for most procedures is safe, but heparin bridging may be useful in selected high-risk patients.

■ COMMENTARY

This is the first report of the use of NOACs peri-

Financial Disclosure: *Clinical Cardiology Alert*'s Editor, Michael H. Crawford, MD, peer reviewer Susan Zhao, MD, Managing Editor Neill Kimball, and Executive Editor Leslie Coplin report no financial relationships relevant to this field of study.

[INSIDE]

Renin-angiotensin system antagonists in stable CAD
page 74

Routine procainamide infusion in the evaluation of patients with cardiac arrest
page 75

Predicting sudden death risk in hypertrophic cardiomyopathy
page 76

FFR in stable coronary artery disease: A second chance at FAME?
page 77

Clinical Cardiology
Critical analysis of the latest clinical research in cardiovascular medicine [ALERT]

Clinical Cardiology Alert, ISSN 0741-4218, is published monthly by AHC Media LLC, One Atlanta Plaza, 950 East Paces Ferry Road NE, Suite 2850 Atlanta, GA 30326.

GST Registration Number: R128870672. Periodicals Postage Paid at Atlanta, GA, and at additional mailing offices.

POSTMASTER: Send address changes to *Clinical Cardiology Alert*, P.O. Box 550669, Atlanta, GA 30355.

SUBSCRIBER INFORMATION
1-800-688-2421
customerservice@ahcmedia.com
www.ahcmedia.com

Questions & Comments:
Please contact Managing Editor **Neill Kimball**, at neill.kimball@ahcmedia.com

Subscription Prices
United States
Print: 1 year with ***free*** *AMA PRA Category 1 Credits™*: $349
Add $19.99 for shipping & handling.
Online only, single user: with ***free*** *AMA PRA Category 1 Credits™*: $299

Multiple Copies: Discounts are available for group subscriptions, multiple copies, site-licenses or electronic distribution. For pricing information, call Tria Kreutzer at 404-262-5482.

Back issues: $42. Missing issues will be fulfilled by customer service free of charge when contacted within one month of the missing issue's date.

Canada: Add 7% GST and $30 shipping.
Elsewhere: Add $30 shipping.

ACCREDITATION
AHC Media is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

AHC Media designates this enduring material for a maximum of ***25*** *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

This CME activity is intended for the cardiologist. It is in effect for 36 months from the date of the publication.

AHC Media

procedurally and provides reassuring data about their safety and effectiveness. The data are similar to a post-hoc analysis of the RE-LY trial of dabigatran vs warfarin, looking at the patients that had a procedure done. Like the RE-LY analysis, this study shows low cardiovascular event rates, which in RE-LY were similar to warfarin. However, this study shows lower major bleeding rates (1.2%) vs RE-LY (4-5%), despite the fact that heparin bridging rates were higher in this study (30%) vs RE-LY (16%). Whether this difference is just due to the different study designs or to the different drugs used is unknown. RE-LY used dabigatran and this registry mainly represented rivaroxaban use (76%) with some dabigatran (23%) and apixaban use (1%).

The data on heparin bridging were also informative in that it did not reduce thromboembolic events, but did seem to increase major bleeding events. These results are somewhat similar to a meta-analysis of warfarin use with heparin bridging that showed reduced thromboembolic events, but increased bleeding (OR = 5). Thus, heparin bridging has been questioned recently. In this study, heparin bridging increased the absolute major bleeding rate, but it was not an independent factor in the multivariate analysis by the authors' definition. A major surgical procedure was the strongest predictor of major bleeding (OR, 16.8; $P < 0.001$); whereas heparin bridging was second (OR, 5; $P = 0.02$). So, concern about the bleeding risks of heparin bridging with NOACs persists and the authors suggest a case-by-case approach. In practice, the main reason to heparin bridge on warfarin therapy has been mechanical prosthetic valves, but NOACs are not indicated for this use, so presumably were not used for such patients in this German study. Thus, the need for heparin bridging with NOACs should be infrequent.

The limitations of this study are that it is observational. Also, the physicians were given no instructions on how to use NOACs. So there could be selection biases. In addition, event rates were low, especially for death. The strengths of the study include the large number of procedures (863), central adjudication of events, and a low rate of lost to follow-up (1%). Thus, until randomized trials are done (unlikely), this study represents the best current data we have on the use of NOACs peri-procedurally. It suggests that it is safe to either continue NOACs for more minor procedures or briefly stop them for more major procedures, and that heparin bridging is usually not needed and may increase bleeding risks. ■

ABSTRACT & COMMENTARY

Renin-angiotensin System Antagonists in Stable CAD

By Michael H. Crawford, MD, Editor

SOURCE: Sorbets E, et al. Renin-angiotensin system antagonists and clinical outcomes in stable coronary artery disease without heart failure. *Eur Heart J* 2014;35:1760-1768.

Renin-angiotensin system antagonists (RASAs) such as angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) have been shown to have beneficial effects in patients with heart failure, reduced left ventricular (LV) systolic function, acute myocardial infarction, hypertension, diabetes, and chronic kidney disease. However, clinical trial results do not consistently show a benefit in stable coronary artery disease (CAD) patients without heart failure or reduced LV function. Part of this trial inconsistency is due to advances in medical care and the fact that trials enter highly selected patient populations that may not reflect the predominant patients seen in practice. Large observational database studies can be of value for shedding light on clinical dilemmas. Thus, this analysis of the Reduction of Atherothrombosis for

Continued Health (REACH) cohort was done to try to clarify the role of RASAs in the management of stable CAD patients without heart failure. The primary combined outcome of REACH was cardiovascular (CV) death, myocardial infarction (MI), or stroke over a 4-year follow-up period. Secondary outcomes included CV hospitalizations for an atherothrombotic event, and tertiary outcomes included all-cause mortality and heart failure. A propensity score adjustment was applied to a multivariate logistic regression model with ACEI/ARB use as the dependent variable. As an internal validity check, the effect of statins on the outcomes was performed in the same manner.

Almost 21,000 patients met the entry requirements, of which about 13,000 were on RASAs and 7500 were not. During a median follow-up of 44 months, 1527 experienced a primary outcome event (12%). The rate of these events was not different between RASA users and non-users (hazard ratio [HR], 1.03; 95% confidence interval [CI], 0.91-1.16; P = 0.66). There were no differences in the secondary or tertiary outcomes. On the other hand, statin use was associated with a lower incidence of the primary outcome (HR 0.74; 95% CI, 0.65-0.83; $P < 0.001$). The authors concluded that the use of RASAs was not associated with beneficial outcomes in stable CAD patients without heart failure.

■ COMMENTARY

Older randomized trials such as HOPE and EUROPA showed benefits from ACEIs in stable CAD patients without heart failure. However, more recent trials such as PEACE and IMAGINE did not. This progression of results suggests that modern evidence-based secondary prevention strategies in CAD patients trumps any potential beneficial effect of RASAs purely for prophylaxis.

There are several strengths to this study. It is very large (almost 21,000 patients) and even without propensity matching, the benefits of RASAs are unimpressive. Also, it is a contemporary international population of patients and the results are consistent over all subsets of the patients. In addition, the analysis of the results of statin therapy performed in the same manner shows a robust benefit in these patients.

There are limitations to this study. Confounding by unmeasured variables is always an issue in observational studies. One prominent issue in this regard is that there was no systemic assessment of LV function. However, if there were patients with unrecognized LV systolic dysfunction, their response to RASAs did not seem to influence the results. The lack of information about the doses of ACEI/ARBs is a problem since trials have shown that their benefit is seen predominantly at higher doses, which may not have been used in this observational study of routine clinical practice. Regardless of these limitations, after seeing the results of PEACE, IMAGINE, and this observational study, I am no longer using RASAs in stable CAD patients without heart failure or LV systolic dysfunction unless another clean cut indication for their use, such as hypertension, is present. ■

ABSTRACT & COMMENTARY

Is There a Role for Routine Procainamide Infusion in the Evaluation of Patients with Cardiac Arrest?

By Edward P. Gerstenfeld, MD

Professor of Medicine, Chief, Cardiac Electrophysiology, University of California, San Francisco

Dr. Gerstenfeld does research for Biosense Webster, Medtronic, and Rhythmia Medical.

SOURCE: Somani R, et al. Procainamide infusion in the evaluation of unexplained cardiac arrest: From the Cardiac Arrest Survivors with Preserved Ejection Fraction Registry (CASPER). *Heart Rhythm* 2014;11:1047-1054.

The Cardiac Arrest Survivors with Preserved Ejection Fraction Registry (CASPER) study evaluated the diagnostic utility of a procainamide infusion test in patients with unexplained cardiac arrest (UCA) or a family history of sudden death (FHSD). Patients with sudden death without any evidence of a Brugada pattern at baseline underwent procainamide testing (15 mg/kg to a maximum of 1 g at 50 mg/min). Patients were excluded if they had impaired left ventricular function (< 50%), any evidence of hypertrophic cardiomyopathy, any epicardial coronary stenosis > 50%, any

anomalous coronary arteries, a prolonged QTc interval, or reversible cause of cardiac arrest. A test was considered positive for Brugada pattern if there was an increase in ST elevation > 1 mm or if there was > 1 mm of new ST elevation in leads V1 and/or V2. Procainamide testing was performed in 174 subjects (age 46.8 ± 15.4 years, 47% female), including 115 UCA survivors. A Brugada pattern was provoked in 12 subjects (6.9%), five of whom had no ST abnormalities at baseline. Ten of the 12 subjects were diagnosed clinically with the Brugada syndrome. Genetic testing was performed in 10 of the 12 procainamide-positive patients and one was positive for a mutation in the SCN5A gene. No subjects with a negative procainamide challenge were subsequently diagnosed with Brugada syndrome. The authors concluded that procainamide testing in subjects with UCA or a FHSD provoked the Brugada ECG pattern in a significant number of subjects, which facilitated the diagnosis of Brugada syndrome and should be recommended in the evaluation of patients with UCA.

■ COMMENTARY

The evaluation of sudden cardiac arrest varies among physicians, often leading to the common endpoint of placement of an implantable cardioverter defibrillator (ICD). In part, this common therapeutic endpoint has led many to limit the evaluation in such patients, since the diagnostic yield is low and therapeutic endpoint often not influenced by the evaluation. Most physicians I have encountered who evaluate a young sudden death survivor will perform an electrocardiogram, echocardiogram, evaluation of the coronary arteries, and then proceed to ICD placement. However, one should not minimize the importance of a more detailed electrophysiology evaluation in such patients. While inherited arrhythmia syndromes are rare, they will have implications not only for the cardiac arrest survivor, but his entire family. A diagnostic electrophysiology study is also imperative, in my opinion. Although uncommon, we have diagnosed several young cardiac arrest survivors with previously undiagnosed accessory pathways leading to rapid supraventricular tachycardia, and even several cases of rapid AV nodal reentry. In the current study, a procainamide infusion was performed in cardiac arrest survivors and their relatives. A Brugada pattern was evoked in 6.9% of patients, including five patients with a completely normal ECG. Although undoubtedly leading to ICD placement, this diagnosis would lead to genetic testing, further evaluation of first-degree relatives, and recommendations to avoid sodium channel blocking drugs such as tricyclic antidepressants and Class IC antiarrhythmics in the cardiac arrest survivor and diagnosed relatives. It seems reasonable that in addition to evaluation of the ECG and coronary arteries, routine electrophysiology study and procainamide infusion should be added to the diagnostic workup of the cardiac arrest survivor, even if the baseline ECG is normal. ■

ABSTRACT & COMMENTARY

Predicting Sudden Death Risk in Hypertrophic Cardiomyopathy

By Michael H. Crawford, MD, Editor

SOURCE: O'Mahony C, et al. A novel clinical risk prediction model for sudden cardiac death in hypertrophic cardiomyopathy (HCM Risk-SCD). *Eur Heart J* 2014;35:2010-2020.

The role of sudden death in hypertrophic cardiomyopathy (HCM) can be ameliorated by an implantable cardioverter-defibrillator (ICD), but the risks of an ICD must be balanced with the risk of sudden death. Traditional clinical risk factors tend to overestimate sudden death risk, hence these investigations at six European centers used data from a retrospective longitudinal cohort study to develop a prognostic model in 3675 patients with clinical HCM (85%) or familial disease. The subjects were ≥ 16 years of age with no history of ventricular arrhythmias, who met standard echocardiographic criteria for HCM and had no other explanation for left ventricular hypertrophy. Sudden death was defined as death within an hour of new symptoms, a nocturnal death, or an appropriate ICD shock in the 15% with ICDs. A prediction equation based on multiple clinical variables was derived from a development population (5 of the 6 centers) and tested in a validation cohort (one of the centers). The new equation was compared to traditional clinical risk factors: severe hypertrophy (wall thickness ≥ 30 mm), nonsustained ventricular tachycardia (NSVT), family history of sudden death, and unexplained syncope. Blood pressure response to treadmill exercise was not included because it has not been independently associated with sudden death.

During a median follow-up of 5.7 years, 5% of the patients experienced sudden death. Six clinical factors that predicted sudden death at the 15% significance level were included in the model: maximal wall thickness, left atrial diameter, left ventricular outflow tract (LVOT) gradient, family history of sudden death, NSVT, and unexplained syncope. The C-Index for the equation was 0.70. If an ICD is placed in 16 patients with a ≥ 4% predicted risk of sudden death, one patient will potentially be saved over 5 years. The authors concluded that this validated risk prediction model for HCM patients provides accurate information about sudden death risk using readily available clinical data.

■ COMMENTARY

The current four or five clinical variables analyzed in a binary fashion are a crude predictor of risk and have been shown to have a low predictive value for sudden death. Their use leads to an overestimation of risk and the placement of ICDs in many low-risk individuals. This new model benefits from a large patient population that is well characterized and includes the full spectrum of HCM patients from severe symptomatic disease to family members identified by echocardiography. It is highly accurate with a C-statistic of 0.70. Using the cutoff of 4% or higher predicted rate of sudden death over 5 years, 71% of the sudden death victims were identified. Also, the formula could be placed online and it could be updated as new information is obtained. Although this is an improvement over our current risk prediction approach, it does have limitations. There is no consensus what constitutes high risk; 4% was chosen here because it most accurately predicted who would have sudden death. Perhaps for clinical purposes a different cutoff would be better. Also, the factors that the investigators included in their initial analysis were only those that had been proven independently predictive in other multivariate studies. Hence, exercise blood pressure response was not included. There may be other variables that would improve the formula; for example, genetic studies and MRI late gadolinium enhancement. In addition, age may be important clinically. In two individuals with identical risk scores, you might treat a 20-year-old differently from a 70-year-old. Although a large diverse population was studied, certain subgroups were poorly represented such as elite athletes, pediatric patients, Asians, and past myectomy or alcohol septal ablation patients. This risk predictor should be used with caution in such patients. Interestingly, once LV wall thickness was > 35 mm, the risk of sudden death fell, so it might not be accurate in this group also. Finally, the effects of various drug therapies were not considered. Many of these issues could be addressed with more data, which could be incorporated into the model. No prediction formula will ever be 100% accurate, but this one seems like a significant step toward more accurate risk prediction in HCM. We await the online version. ■

ABSTRACT & COMMENTARY

FFR in Stable Coronary Artery Disease: A Second Chance at FAME?

By Jeffrey Zimmet, MD, PhD

Associate Professor of Medicine, University of California, San Francisco, Director, Cardiac Catheterization Laboratory, San Francisco VA Medical Center

Dr. Zimmet reports no financial relationships relevant to this field of study.

SOURCE: De Bruyne B, et al. Fractional flow reserve-guided PCI for stable coronary artery disease. *N Engl J Med* 2014; Sep 1. [Epub ahead of print.]

In acute coronary syndromes, percutaneous coronary intervention (PCI) has clear benefits in terms of hard clinical endpoints. In the realm of stable coronary disease, however, optimal medical therapy has for some time now taken center stage, with PCI relegated to a supporting role whose primary purpose is to treat symptoms. This is based on a number of research studies, most prominently the 2007 Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial, which reported that PCI driven by angiography is no better than medical therapy alone at preventing clinical outcomes including death and myocardial infarction (MI). In addition to using angiography to drive treatment decisions, COURAGE used primarily older, bare-metal stents for treatment. Since the original FAME trial was published in 2009, fractional flow reserve (FFR) has gained significant traction as a more objective means (compared with angiography alone) to determine the ischemic potential of epicardial

stenoses. The Fractional Flow Reserve versus Angiography for Multivessel Evaluation 2 (FAME 2) trial was designed to compare medical therapy with PCI using modern techniques and second-generation drug-eluting stents in patients with stable CAD and functionally significant coronary lesions as defined by FFR.

Although 2-year outcomes were pre-specified in the trial design, the study was stopped early after an average follow-up of only 7 months due to an excess of urgent revascularization in the medical therapy group. Death and MI were not significantly different between the groups. The problem with the early termination decision and subsequent criticism of the published result seems obvious — physicians as well as patients were aware of the cardiac cath findings and study group assignments, which clearly could have lowered the threshold for urgent revascularization in the medical therapy arm.

De Bruyne and colleagues now present the long-awaited 2-year follow-up data from the FAME 2 trial. In the trial, 888 patients with 1601 PCI-eligible lesions were enrolled. These patients were randomized to undergo FFR-guided PCI plus medical therapy (447 patients) or to receive medical therapy alone. The primary endpoint was a composite of death from any cause, nonfatal MI, or unplanned hospitalization leading to urgent revascularization within 2 years. As with the early data, the most striking difference between groups was a 77% reduction in urgent revascularization in the PCI group, as compared with the medical-therapy group (4.0% vs 16.3%; hazard ratio [HR], 0.23; 95% CI, 0.14-0.38; $P < 0.001$). While more than half of these urgent revascularization decisions were prompted by clinical presentation alone, there was also a lower incidence of revascularization triggered by MI or ECG changes in the PCI group compared with the medical therapy group (3.4% vs 7.0%; $P = 0.01$). More importantly, when excluding periprocedural MI, patients in the PCI group had a 44% relative risk reduction for the composite of death or MI (4.6% vs 8.0%; HR, 0.56; 95% CI, 0.32-0.97; $P = 0.04$). As expected for this stable CAD population, mortality was low (mean of 1.4%) and did not show a significant difference between groups.

■ COMMENTARY

How will these results change practice? Will we now concede that PCI in stable coronary disease has the potential to change hard clinical outcomes? While these results are compelling and thought provoking, several points are worth noting. The authors of the study argue quite convincingly that urgent revascularization represents a failure of the assigned treatment, and the accompanying editorial dubs this "a viable hard end point." Nonetheless, the unblinded nature of the study leaves open the probability that awareness of a functionally significant stenosis influenced decision making of the physician or the patient during follow-up. And while just over 40% of patients in the medical-therapy group had crossed over to undergo PCI by 2 years, this also suggests that nearly 60% of these patients with FFR-positive stenoses did fine without revascularization. This would seem to buttress the argument for an initial strategy of medical therapy in stable coronary disease.

It is important to recognize that the between-group difference reported in death or MI was not significant for the data set as a whole. A significant difference was only measured by excluding data from the first 7 days following randomization, which effectively cordoned off periprocedural MI events. While the authors contend that "periprocedural infarctions rarely have an effect on the long-term prognosis for patients undergoing PCI," the relatively stringent definition of MI used in this trial (10× the upper limit of normal in the CK-MB or an increase by a factor of more than 5 when accompanied by objective evidence of tissue loss) supplies a basis for criticism of this premise. In the end, we are left with some very intriguing food for thought, but without a clear answer that is likely to change practice guidelines. ■

ABSTRACT & COMMENTARY

Prehospital Ticagrelor Administration in STEMI Patients Falls Short

By Jeffrey Zimmet, MD, PhD

Associate Professor of Medicine, University of California, San Francisco, Director, Cardiac Catheterization Laboratory, San Francisco VA Medical Center

SOURCE: Montalescot G, et al. Prehospital ticagrelor in ST-segment elevation myocardial infarction. *N Engl J Med* 2014;371:1016-1027.

The preferred treatment for patients presenting with ST-segment elevation myocardial infarction (STEMI) is primary percutaneous coronary intervention (PCI). Optimization of pharmacotherapy before, during, and after primary PCI has the potential to improve outcomes. Antiplatelet therapy with both aspirin and P2Y12 inhibitors such as clopidogrel is a cornerstone of treatment for PCI. In the setting of acute coronary syndromes, more potent inhibition of the platelet P2Y12 receptor with newer agents including ticagrelor and prasugrel has been shown to reduce downstream ischemic events. The results with ticagrelor were particularly positive in the STEMI subgroup of the PLATO trial. These results were seen with in-hospital administration of the drug; whether earlier administration would be beneficial was not known.

The ATLANTIC study sought to answer the following question: In STEMI patients, does pre-hospital administration of ticagrelor have an advantage over later administration in the cardiac catheterization laboratory in terms of efficacy of coronary reperfusion? In the current environment, where both upstream and intraprocedural use of glycoprotein IIb/IIIa inhibitors in STEMI has been waning, this is a constructive inquiry. To answer this, Montalescot and colleagues randomized 1862 patients presenting with STEMI of < 6 hours' duration to receive ticagrelor either in the ambulance or in the hospital. As primary endpoints, they chose to look at ST-segment resolution pre-PCI, as well as the percentage of patients who did not have normal (TIMI grade 3) flow in the infarct artery at the time of initial angiography. These endpoints mirror those that have shown significant changes in prior studies of upstream use of glycoprotein inhibitors in STEMI. Multiple secondary endpoints were also prespecified, including rates of major adverse cardiovascular events and definite stent thrombosis at 30 days, and ST-segment resolution and TIMI 3 flow at the end of the PCI procedure. The makers of ticagrelor, AstraZeneca, sponsored the study.

During the study, an impressive 1862 patients out of the 1875 enrolled provided written informed consent. A total of 909 patients were randomly assigned to prehospital ticagrelor, while 953 were assigned to receive the drug later in the hospital. This was a mammoth undertaking involving 102 ambulance services and 112 PCI centers in 13 countries. The median time from symptom onset to diagnostic ECG was 78 minutes, while the time from randomization to cardiac catheterization averaged a swift 48 minutes. The median time difference in ticagrelor administration between the pre-hospital and in-hospital groups was only 31 minutes.

In terms of the primary endpoint, the earlier administration of ticagrelor had no significant effect — neither ST-segment resolution nor occurrence of TIMI 3 flow by the time of initial angiography was significantly affected. The combined secondary endpoint, including the composite of death, MI, stroke, urgent revascularization, and stent thrombosis, was not significantly different between the groups. In an interesting twist, however, stent thrombosis at both 24 hours (0 of 906 patients [0%] in the prehospital group vs 8 of 952 [0.8%] in the in-hospital group, $P = 0.008$) and 30 days (2 of 906 [0.2%] vs 11 of 952 [1.2%], $P = 0.02$) was significantly reduced in the early ticagrelor group. As might be expected, there was no difference in bleeding related to the timing of ticagrelor administration.

■ COMMENTARY

In 2001, Dr. Montalescot published the ADMIRAL study, in which 300 patients with STEMI were randomized to receive either the glycoprotein IIb/IIIa inhibitor abciximab or placebo prior to cardiac catheterization. The abciximab group showed a remarkable benefit both in terms of pre-PCI vessel patency as well as 30-day clinical outcomes. More recent STEMI trials of upstream IIb/IIIa inhibitor use, such as the influential ON-TIME2 study, showed positive effects on ST-segment resolution but not on clinical endpoints. Is it surprising that the current study failed in its primary endpoints? Not really. Much has changed since the ADMIRAL study more than a decade ago. One important difference comes from the door-to-balloon effort that has so dramatically shortened the time to cardiac catheterization. In ATLANTIC, the difference in time of ticagrelor administration between the pre- and in-hospital groups was a scant 31 minutes. Looking for a difference in vessel patency so shortly after administration of an oral agent, even a very potent one such as ticagrelor, seems like a lot to expect. In addition, approximately 30% of patients received a glycoprotein IIb/IIIa inhibitor before PCI, further blunting the effect of ticagrelor timing.

ATLANTIC was not a complete bust, however. Although the numbers were small, the positive effect on early stent thrombosis was clear. And this effect is biologically plausible, especially in the environment where IIb/IIIa inhibitors are used in a minority of cases. All by itself, this is a good reason to consider giving ticagrelor or alternate antiplatelet agents as soon as practicable in cases of confirmed STEMI. ■

QUESTIONS & COMMENTS:
Contact Neill Kimball, Managing Editor, at (404) 262-5404 or email at neill.kimball@achmedia.com between 8:30 a.m. and 4:30 p.m. ET, Monday-Friday.

CME INSTRUCTIONS

To earn credit for this activity, please follow these instructions:
1. Read and study the activity, using the provided references for further research.
2. Scan the QR code to the right or log on to **www.cmecity.com** to take a post-test; tests can be taken after each issue or collectively at the end of the semester. First-time users will have to register on the site using the 8-digit subscriber number printed on their mailing label, invoice or renewal notice.
3. Pass the online tests with a score of 100%; you will be allowed to answer the questions as many times as needed to achieve a score of 100%.
4. After successfully completing the last test of the semester, your browser will be automatically directed to the activity evaluation form, which you will submit online.
5. Once the completed evaluation is received, a credit letter will be e-mailed to you instantly.

CME QUESTIONS

1. In-ambulance vs pre-PCI ticagrelor administration in STEMI patients resulted in:
a. greater ST-elevation regression.
b. more TIMI-3 flow to the infarct artery.
c. less early in-stent thrombosis.
d. increased major bleeding events.

2. In stable CAD patients, ischemia-guided PCI compared to optimal medical therapy alone results in:
a. less subsequent urgent revascularization.
b. reduced mortality.
c. reduced MI rate.
d. All of the above

3. Sudden death in hypertrophic cardiomyopathy is known to be associated with:
a. exercise-induced hypertension.
b. LV wall thickness > 3.5 cm.
c. a Valsalva-induced LV outflow gradient.
d. unexplained syncope.

4. In stable CAD patients with normal systolic LV function, renin-angiotensin system blockers:
a. improved survival.
b. reduced MI rate.
c. reduced stroke rate.
d. None of the above

5. Continuation or brief interruption of new oral anticoagulants periprocedure vs heparin bridging is associated with:
a. more cardiovascular events.
b. more major bleeding.
c. higher costs.
d. None of the above

6. Patients with unexplained cardiac arrest should have a:
a. cardiac MRI.
b. procainamide infusion challenge.
c. head up tilt table test.
d. signal averaged ECG.

CME OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- discuss the most current information related to cardiac illness and the treatment of cardiac disease;
- explain the advantages and disadvantages, as well as possible complications of interventions to treat cardiac illness;
- discuss the advantages, disadvantages, and cost-effectiveness of new and traditional diagnostic tests in the treatment of cardiac illness; and
- discuss current data regarding outpatient care of cardiac patients.