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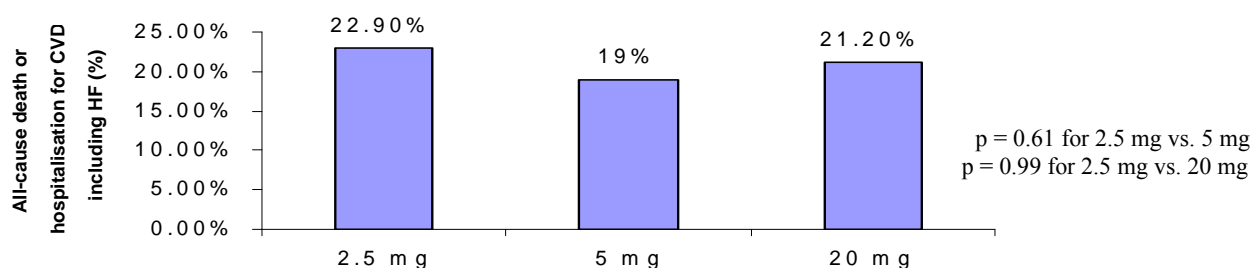
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J-CHF study: Lower doses of carvedilol as effective as higher recommended doses in CHF

Results of the Japanese-Chronic Heart Failure (J-CHF) study showed that patients benefited from lower doses of the beta-blocker carvedilol and suggested that tailoring the dose of the drug to the individual patient's response is better than a "one-size-fits-all" approach. **This trial was presented during the late-breaking clinical trial sessions at the American Heart Association Scientific Sessions.**

The goal of this trial was to compare three doses of carvedilol among patients with chronic stable heart failure. The study was randomized, blinded and parallel in design. Dr. Masatsugu Hori, MD (Osaka Medical Center for Cancer and CVD, Japan), the lead investigator, enrolled 364 patients with NYHA II or III HF and assigned them to one of three dosages of carvedilol: 2.5 mg (n=119), 5 mg (n=121) and 20 mg (n=120). There were no real differences in baseline characteristics in patients.

During three years of follow-up, 20% of patients reached the primary endpoint of all-cause death or hospitalization for cardiovascular disease (CVD) including heart failure (HF). The researchers reported no statistically significant difference between the three groups. The number of all-cause deaths (n) was 9, 7, and 8; hospitalization for CVD was 8, 10, and 5; and hospitalization for HF was 21, 14, and 18 (p = NS for outcomes). LVEF increased from 30% to 43% in groups (p < 0.05 for intragroup comparisons).



However, 23% of patients assigned to 20 mg per day had to discontinue or change their dose due to adverse effects compared with only 2% in the 2.5 mg group and 4.2% in the 5 mg group. In the 20 mg group, patients experienced more hypotension and bradycardia (11.2%) than in the 2.5 mg group (3.4%) or 5 mg group (6%). Carvedilol use was discontinued in 3.4% of the 20 mg group, 2.6% of the 5 mg group and 1.7% of the 2.5 mg group. The proportion of patients that required a change in treatment dose was 0.7% for the 2.5 mg group, 4.2% for the 5 mg group, and 23% for the 20 mg group (p < 0.05).

In most Western countries, 50 mg to 100 mg per day is recommended, said Dr. Hori. But based on the MUCHA (Multicenter Carvedilol Heart Failure Dose Assessment) trial conducted in Japan, a small dose of 5 mg to 20 mg of carvedilol is recommended as the maintenance dose. **“J-CHF suggests initiating carvedilol at the lowest dose and increasing the dose incrementally until the desired reductions in heart rate and/or plasma brain natriuretic peptide are achieved,”** according to Hori.

The optimal dose of a beta-blocker in patients with chronic stable heart failure remains an important question. Unfortunately, this study was significantly underpowered to detect a difference in important clinical outcomes.

HEAAL study reveals: High-dose ARB therapy better than low-dose, in HF patients intolerant to ACE inhibitors

The Heart Failure End Point Evaluation of Angiotensin II Antagonist Losartan (HEAAL) study presented at the *American Heart Association 2009 Scientific Sessions* & simultaneously published online in the *Lancet*, showed that **150 mg/day dosage of losartan significantly reduced the risk of death or heart-failure hospitalization compared to losartan 50 mg/day in systolic heart failure patients who couldn't tolerate ACE inhibitors.**

In the study, 3846 patients in 30 countries who had New York Heart Association (NYHA) class II-IV heart failure, left ventricular ejection fraction (LVEF) <40%, and intolerance of ACE inhibitors were randomized to receive losartan at either 150 mg/day (n=1921) or 50 mg/day (n=1913). In the high-dose group, up-titration from 50 mg/day was done over the period of three weeks. ACE-inhibitor intolerance was due to cough in 86% of cases.

Over a median follow-up of 4.7 years, the **incidence of primary end point i.e. rates of death or heart failure hospitalization was 43% in the high-dose group & 46% in the low-dose group. The difference was modest but significant & it was majorly driven by a significant 13% risk reduction of heart failure hospitalization observed with 150 mg/day dose of losartan vs 50 mg/day dose** (Table 1).

Table 1: Risk reduction for end points, high-dose vs low-dose losartan

End point	Risk Reduction	P value
Death or heart failure hospitalization	10 %	0.027
All-cause death	6 %	0.24
Heart failure hospitalization	13 %	0.025
CV hospitalization	11 %	0.023

Interestingly, patients without a history of hypertension showed a significant 23% greater risk reduction with losartan at 150 mg/day than 50 mg/day vs those with a history of hypertension. Mean systolic and diastolic blood pressure was reduced significantly in both treatment groups by six months, but heart rate did not.

However, at the end of one year, mean serum potassium significantly increased by 0.02 mmol/L in the high-dose group and dropped by 0.01 mmol/L in the low-dose group. The estimated glomerular filtration rate fell significantly in the two groups by 6.1 mL/min/1.73 m² and 1.9 mL/min/1.73 m² respectively. **Although the high-dose group experienced more renal dysfunction, hypotension, and hyperkalemia, it didn't lead to significantly more treatment discontinuation.**

The study author, Dr Marvin A Konstam, Tufts University, Boston, MA, said that the present findings, along with the results of other trials, make a **strong case for the value of incremental inhibition of the renin-angiotensin system (RAS).** He added that **similar benefit could be achieved by increasing the dose of a particular agent, rather than by addition of an additional class of agent,** although he agrees the need of future studies to test this hypothesis.

In an accompanying editorial, Dr Henry Krum, Monash University, Melbourne, points that the small increment of serious adverse events in HEAAL (specifically in those patients who had to be withdrawn from therapy) seems a reasonable trade-off for the potential increased therapeutic benefit of the higher ARB dose. However he cautions against applying the findings to patients who can take ACE inhibitors, as HEAAL did not provide any information about whether a high-dose ARB is better than an ACE-inhibitor strategy nor did it offer insights about whether maximizing the dose of one RAS blocker is better than use of several agents or whether it would be beneficial to add the 150-mg/day ARB to an ACE inhibitor.

RELY trial: Dabigatran as an Alternative to Warfarin May Cut Risk of Bleeding

The anticoagulant, dabigatran etexilate may be more effective and safer than warfarin at preventing clots and stroke in patients with atrial fibrillation, as per the RELY study presented at the *American Heart Association Scientific Sessions 2009*.

Warfarin is effective in preventing blood clots that can cause stroke in patients with atrial fibrillation and other diseases, but the drug has a narrow therapeutic range in which it prevents strokes but doesn't cause bleeding, according to the researchers. This means that effective warfarin treatment requires regular laboratory monitoring to ensure warfarin levels remain in the range that lowers the risk of stroke without increasing the risk of bleeding.

The RELY study included 18,113 atrial fibrillation patients in 44 countries. Patients were randomized to one of two doses of dabigatran (110 mg, n = 6,015; 150 mg, n = 6,076; blinded to study drug dose) or to open-label warfarin (n = 6,022). Warfarin could be dose-adjusted to a target international normalized ratio (INR) of 2.0-3.0; INR was to be measured at least monthly.

The primary endpoint of stroke or systemic embolism occurred in 1.53%/year in the dabigatran 110 mg group and 1.11%/year in the dabigatran 150 mg group compared with 1.69%/year in the warfarin group, meeting the criteria for noninferiority in both groups. The dabigatran 150 mg group also met superiority criteria (relative risk [RR] 0.66, 95% confidence interval [CI] 0.53-0.82, $p < 0.001$), but the dabigatran 110 mg group did not (RR 0.91, 95% CI 0.74-1.11, $p = 0.34$). This finding remained the same, irrespective of the degree of INR control at individual centers.

The secondary endpoint of stroke was also significantly lower in the dabigatran 150 mg group (1.01%/year) compared with warfarin (1.57%/year, RR 0.64, 95% CI 0.51-0.81, $p < 0.001$), but the dabigatran 110 mg group was not (1.44%/year, RR 0.92, 95% CI 0.74-1.13, $p = 0.41$). Both doses of dabigatran had a lower rate of hemorrhagic stroke compared with warfarin (RR for 150 mg 0.26, 95% CI 0.14-0.49, $p < 0.001$; RR for 110 mg 0.31, 95% CI 0.17-0.56, $p < 0.001$). Compared to the warfarin group, myocardial infarction trended higher with both dabigatran 150 mg (0.74%/year vs. 0.53%/year, RR 1.38, 95% CI 1.00-1.91, $p = 0.048$) and dabigatran 110 mg (0.72%/year, RR 1.35, 95% CI 0.98-1.87, $p = 0.07$).

Death from vascular causes was lower in the dabigatran 150 mg group (2.28%/year) compared with warfarin (2.69%/year, RR 0.85, 95% CI 0.72-0.99, $p = 0.04$), but the dabigatran 110 mg group was not (2.43%/year, RR 0.90, 95% CI 0.77-1.06, $p = 0.21$). Results were similar for all-cause mortality: warfarin 4.13%/year, dabigatran 150 mg group 3.64%/year (RR 0.88, 95% CI 0.77-1.00, $p = 0.051$), dabigatran 110 mg 3.75%/year, (RR 0.91, 95% CI 0.80-1.03, $p = 0.13$).

The primary safety endpoint of major bleeding occurred at a rate of 3.36%/year in the warfarin group, which was higher than in the dabigatran 110 mg group (2.71%/year, RR 0.80, 95% CI 0.69-0.93, $p = 0.003$), but did not differ from the dabigatran 150 mg group (3.11%/year, RR 0.93, 95% CI 0.81-1.07, $p = 0.31$). GI bleeding was more frequent in the dabigatran 150 mg group compared with warfarin (1.51%/year vs. 1.02%/year, $p < 0.001$). Both doses of dabigatran had significantly lower rates of major or minor bleeding compared with warfarin (14.62%/year for dabigatran 110 mg, 16.42%/year for dabigatran 150 mg and 18.15%/year for warfarin). Bleeding outcomes remained the same, irrespective of the degree of INR control at individual centers.

The net clinical benefit outcome, which was a composite of stroke, systemic embolism, pulmonary embolism, myocardial infarction, death, or major bleeding, favored the dabigatran 150 mg group over warfarin (RR 0.91, 95% CI 0.82-1.00, $p = 0.04$), but did not differ between the dabigatran 110 mg group versus warfarin (RR 0.92, 95% CI 0.84-1.02, $p = 0.10$). Dyspepsia

occurred more frequently with dabigatran than warfarin (11.8% in the 110 mg group and 11.3% in the 150 mg group vs. 5.8% in the warfarin group, $p < 0.001$). There was no difference in liver function tests.

The study concluded that In patients with atrial fibrillation, dabigatran given at a dose of 110 mg was associated with rates of stroke and systemic embolism that were similar to those associated with warfarin, as well as lower rates of major hemorrhage. Dabigatran administered at a dose of 150 mg, as compared with warfarin, was associated with lower rates of stroke and systemic embolism but similar rates of major hemorrhage.

Adapted from: www.cardiosource.com as accessed on November 16, 2009

PLATO study: Novel antiplatelet agent Ticagrelor better as compared to clopidogrel in ACS

Among patients with STE or non-STE ACS, treatment with the novel reversible oral P2Y12 receptor antagonist ticagrelor significantly reduced the composite endpoint of death from vascular causes, MI, or stroke by 12 months compared with clopidogrel, without an excess in the primary safety endpoint of major bleeding as shown by the the PLATElet inhibition and patient Outcomes (PLATO) study.

Current guidelines recommend dual antiplatelet treatment with the thienopyridine clopidogrel in addition to aspirin in patients with ACS. However, limitations of clopidogrel include that it is a prodrug with delayed onset of action, has large interpatient variability, and has irreversibility of its platelet inhibition effects. Lead investigator Lars Wallentin (Uppsala University, Sweden) emphasized that ticagrelor is the second novel P2Y12 receptor antagonist (after prasugrel) to undergo large-scale testing with promising results compared to clopidogrel.

The goal of the trial was to evaluate the safety and efficacy of treatment with ticagrelor compared with clopidogrel among patients with an acute coronary syndrome (ACS) with or without ST-segment elevation. Patients were randomized to ticagrelor (n = 9,333; loading dose 180 mg followed by 90 mg twice daily) or clopidogrel (n = 9,291; loading dose 300 mg followed by 75 mg daily), for up to 12 months. An additional dose of study drug was given at the time of percutaneous coronary intervention (PCI) for those undergoing PCI following randomization. Patients were loaded with 325 mg aspirin. If tolerated, all patients received aspirin 75-100 mg daily if no stent was placed and 325 mg daily (for 6 months) if stent was placed.

End point	PLATO STEMI results		Hazard ratio for ticagrelor	p
	Ticagrelor (%)	Clopidogrel (%)		
Primary end point: death from vascular causes, MI, or stroke	9.3	11.0	0.85	0.02
Secondary end points				
All-cause mortality	4.9	6.0	0.82	0.04
CV mortality	4.5	5.4	0.84	0.09
Definite stent thrombosis	1.6	2.5	0.61	0.01
MI	4.7	6.1	0.77	0.01
Primary safety event: major bleeding	9.0	9.3	0.96	0.63

Discontinuation of study drug was slightly higher in the ticagrelor group (23.4% vs. 21.5%, p = 0.002). In terms of side effects other than bleeding, dyspnea was seen more frequently with ticagrelor than with clopidogrel (12.9% vs 8.3%; p<0.0001), but discontinuations due to this side effect were very low (0.5% vs 0.1%; p=0.0003).

The investigators speculated that “the improved survival rate with ticagrelor might be due to the decrease in the risk of thrombotic events without a concomitant increase in the risk of major bleeding” seen with clopidogrel and prasugrel. Commenting on the trial, Freek Verheugt (University of Nijmegen Medical Centre, The Netherlands) said the results of PLATO represented a “dream finding” of improved thrombotic event reduction without an overall excess bleeding risk, likely relating to ticagrelor’s distinct pharmacology. Ticagrelor is a more potent inhibitor of platelet aggregation than clopidogrel, but inhibits platelet (P2Y12) activity reversibly, as opposed to the irreversible inhibition achieved with clopidogrel and prasugrel, with a rapid onset and offset of action. He said that PLATO “will change the practice, change the guidelines, and is quite definitive.”

In an accompanying editorial in the *NEJM*, Albert Schömig proposed that **the availability of clopidogrel, prasugrel, and ticagrelor “may make it possible to individualize antiplatelet therapy.”** Ticagrelor, he wrote, “may be preferred in patients whose coronary anatomy is unknown and for whom a CABG procedure is deemed probable.”

N Engl J Med 2009; 361:1045-57
N Engl J Med 2009; 361:1108-11

NIA Plaque: Niacin Not Beneficial in Patients at Goal With Statins

According to the NIA Plaque study, the addition of niacin to statin therapy in secondary-prevention patients resulted in a significant improvement in LDL- and HDL-cholesterol levels but failed to significantly alter atherosclerotic disease progression as measured by MRI, compared with statin therapy alone. The results were presented by Dr Christopher Sibley (Johns Hopkins University Medical Center, Baltimore, MD) on November 18, 2009 at the *American Heart Association (AHA) 2009 Scientific Sessions*.

The trial was designed to determine whether there would be any additional benefit of raising HDL-cholesterol levels on atherosclerotic disease progression in older secondary-prevention patients, compared with optimizing statin therapy.

In total, 145 patients with clinically evident atherosclerosis were randomized to 1500 mg daily of extended-release niacin or to placebo. All patients were treated with a statin as needed to reach NCEP ATP III LDL-cholesterol targets. After 18 months of follow-up, extended-release niacin resulted in significant increases in HDL cholesterol and a significant decrease in LDL cholesterol. Statins alone resulted in significant reductions in LDL cholesterol but did not positively affect HDL-cholesterol levels.

NIA Plaque: Change in Lipid Parameters From Baseline to 18 Months

Lipid measure (mg/dL)	Statin + placebo, baseline	Statin + placebo, 18 mo	Statin + extended-release niacin, baseline	Statin + extended-release niacin, 18 mo	p (between groups)
Total cholesterol	166	152	174	150	0.65
LDL cholesterol	86	77	88	67	0.03
HDL cholesterol	55	49	55	58	<0.001
Triglycerides	123	93	115	84	0.02

Regarding the primary end point, the change in the internal carotid artery wall volume, both treatment strategies resulted in significant reductions from baseline, but there was no significant difference between the two treatment arms, nor were there any significant differences between treatments for numerous secondary MRI outcomes, including measurements of the lipid core.

"It's essentially a win for the National Cholesterol Education Program Adult Treatment Panel III [NCEP ATP III] guideline, focusing on LDL lowering with statin therapy. Previous trials have certainly shown that niacin has multiple effects, and we know it affects multiple lipid parameters, but our results show that those effects were effectively dwarfed by the effects of the statin," said Sibley.

The results, from the NIA Plaque study, are in contrast with the findings from the Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol: HDL and LDL Treatment Strategies in Atherosclerosis (ARBITER 6-HALTS) study which states that niacin helped with plaque regression when used on top of optimized statin therapy.

This difference in the result could be attributed to the difference in the patient population of the two studies. Patients in NIA Plaque were older and had less diabetes mellitus and glucose intolerance, but, most important, had higher HDL-cholesterol levels when randomized to extended-release niacin than those in the ARBITER 6 study. The average baseline HDL cholesterol in the NIA Plaque study was 55mg/dL, higher than the 42 mg/dL in the ARBITER 6-HALTS study.

"Those studies show a beneficial effect of extended-release niacin in general, but we studied patients above the low HDL-cholesterol cap," said Sibley. "In terms of expanding the use to a more general population, the results do not support it."

Adapted from www.theheart.org as accessed on November 19, 2009.

ARBITER 6-HALTS: Niacin superior to ezetimibe

Adding extended-release niacin to statin therapy results in a significant regression of atherosclerosis as measured by carotid intima-media thickness (IMT), whereas the addition of ezetimibe to statin therapy did not, as per the results of the **Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol 6: HDL and LDL Treatment Strategies in Atherosclerosis** (ARBITER 6-HALTS) study, presented on November 15, 2009 at the *American Heart Association 2009 Scientific Sessions* and published simultaneously online in the *New England Journal of Medicine*.

In the ARBITER 6-HALTS study, investigators compared two distinct lipid-modifying strategies in patients who had or who were at high risk for vascular disease but who had LDL-cholesterol levels <100 mg/dL and moderately low HDL-cholesterol levels (<50 mg/dL).

In the trial, 363 patients were enrolled, half were randomized to a treatment that further reduced LDL-cholesterol levels with the addition of ezetimibe (10 mg/daily) to statin therapy, while the other half were randomized to HDL-raising therapy with extended-release niacin (2000 mg/daily). At baseline, the mean LDL-cholesterol level was 84 mg/dL and 81 mg/dL in the niacin- and ezetimibe-treatment arms, respectively. The primary study endpoint was the between-group difference in the change from baseline in the mean common carotid intima-media thickness.

According to the study results, the mean HDL level increased by 18.4% during the 14-month study period in the niacin group ($P<.001$) and mean LDL decreased in the ezetimibe group decreased by 19.2% ($P<.001$). Niacin was more efficacious than ezetimibe for the change in carotid intima-media thickness over the study period ($P=0.003$). The researchers reported that niacin therapy caused a reduction in the mean and the maximal carotid intima-media thickness at both eight and 14 months, while no significant net changes in carotid intima-media thickness were reported in the ezetimibe group.

Stein, a researcher with experience in IMT studies, said the amount of regression with niacin is significant. "The difference between niacin and ezetimibe in the IMT measurements is very large. The difference of 0.017 mm over 14 months is on the order of statin therapy vs placebo. It is essentially as effective as a statin and would be expected to translate into a large difference in cardiovascular events, which was observed in this study."

"The results of ARBITER 6-HALTS and a number of other clinical trials support the concept that the use of statins to reduce LDL to target and the subsequent addition of niacin (LDL lowering plus HDL-increasing), as compared with ezetimibe (only LDL lowering), will provide more effective treatment of the high-risk patient," said by John J.P. Kastelein, MD, PhD, Professor of medicine, Academic Medical Centre, University of Amsterdam.

Thus, the results available to date provide support for the concept that the use of statins to reduce LDL to target levels with the subsequent addition of a drug to raise HDL-cholesterol levels (niacin), rather than a drug to lower LDL-cholesterol levels (ezetimibe), is a more effective treatment for patients at high cardiovascular risk.

Adapted from www.theheart.org as accessed on November 16, 2009

POPE study: Diclofenac not useful for reducing pericardial effusion

Routinely giving a non-steroidal anti-inflammatory drug (NSAID), diclofenac, was not effective at treating moderate to severe pericardial effusion in patients following cardiac surgery and researchers recommend discontinuing use, according to data presented from the *Non-steroidal Anti-Inflammatory Treatment for Post-operative Pericardial Effusion (POPE)* trial.

“Our results confirm that moderate to severe pericardial effusion is a very serious condition as 10% of these patients will require pericardial drainages in the two weeks following surgery,” Philippe Meurin, MD (Villeneuve Saint Denis, France), the principal investigator, said during a press conference. The amount of fluid build-up early on can predict the likelihood of cardiac tamponade. NSAIDs are widely prescribed after heart surgery in order to try to reduce the volume of these effusions, but no study prior to this one has assessed their usefulness in this indication. In addition, numerous studies have indicated potential drawbacks from using NSAIDs, including gastrointestinal bleeding, particularly in patients on antiplatelet agents. Therefore, it seemed important to assess the benefit/risk balance of using these drugs after heart surgery.

Meurin and colleagues set out to assess whether or not diclofenac was effective at reducing post operative pericardial effusion volume in 196 patients with moderate to large amounts of fluid around the heart within one month following cardiac surgery. The multi-center, double-blind, placebo-controlled POPE study randomly assigned the patients to receive 100 mg per day of the NSAID diclofenac or a placebo for 14 days. **After 14 days of treatment, data indicated a mean pericardial effusion grade decrease of -1.08 in patients assigned to placebo vs. -1.36 patients assigned to diclofenac ($P=.15$). It also failed to prevent the serious problem of cardiac tamponade.**

“These results highlight the fact that sometimes it is useful to design clinical studies to determine whether our longstanding habits are truly appropriate for patients’ health,” said Meurin. “We believe that prescribing an NSAID to treat an asymptomatic post-operative fluid build-up around the heart should no longer be advised,” he said. “It seems to be useless in this clinical setting,” Meurin concluded.

*Adapted from <http://www.cardiologytoday.com/view.aspx?rid=50614>
<http://americanheart.mediaroom.com/index.php?s=43&item=891> as accessed on 17th November 2009*

TREAT study: Darbepoetin alfa provides no CV event reduction in anemic kidney disease patients with diabetes

The administration of darbepoetin alfa was not associated with a reduction in death, cardiovascular events or end-stage renal disease, according to results of the Trial to Reduce Cardiovascular Events With Aranesp Therapy (TREAT) trial. The researchers also reported elevated rates of stroke in patients receiving darbepoetin vs. placebo.

Although erythropoiesis-stimulating agents (ESAs) are widely used in patients with anemia and chronic kidney disease (CKD) who are not on dialysis, randomized data to support this approach are not available. The TREAT trial sought to test the hypothesis that the use of ESAs in patients with diabetes and CKD who were also anemic would be associated with improved outcomes. It was a placebo-controlled, randomized, blinded, parallel and stratified study. Researchers enrolled 4,038 patients with type 2 diabetes, chronic kidney disease and concomitant anemia in the study and randomly assigned them to either receive darbepoetin alfa (n=2,012) or placebo (n=2,026). Baseline characteristics were fairly similar between the two groups, except for a history of congestive heart failure (CHF), which was lower in the darbepoetin alfa arm (p = 0.01).

From 3 months to the end of follow-up (median of 29.1 months), the median Hgb was higher in the darbepoetin alfa arm (12.5 vs. 10.6 g/dl). Over the course of the study, 46% of the patients assigned to placebo received at least one dose of darbepoetin alfa as rescue therapy. Red blood cell transfusion was lower in the darbepoetin alfa arm as compared with placebo (14.8% vs. 24.5%, p < 0.001). **The primary endpoint of death, myocardial infarction (MI), unstable angina, heart failure, or stroke was similar between the darbepoetin alfa and placebo arms (31.4% vs. 29.7%, hazard ratio 1.05, 95% confidence interval 0.94-1.17, p = 0.41).** Individual endpoints such as all-cause mortality (20.5% vs. 19.5%, p = 0.48) and MI (6.2% vs. 6.4%, p = 0.73) were similar between the two arms, **except stroke (5% vs. 2.6%, p < 0.001), which was higher in the darbepoetin alfa arm. The renal composite endpoint of ESRD or death was similar between the two arms (32.4% vs. 30.5%, p = 0.29).** Similarly, the incidence of ESRD was similar between the two arms (16.8% vs. 16.3%, p = 0.83).

Diastolic blood pressure was higher in the darbepoetin alfa arm (median: 73 vs. 71 mm Hg, p < 0.001). There was a trend toward a higher incidence of hypertension in the darbepoetin alfa arm (p = 0.07). Venous (2.0% vs. 1.1%, p = 0.02) and arterial (8.9% vs. 7.1%, p = 0.04) thromboembolic events were more frequent in the darbepoetin alfa arm. There was no difference in the incidence of cancer between the two arms (p = 0.53).

“In patients with type 2 diabetes and chronic kidney disease who are not on dialysis and who have anemia, the strategy to treat their anemia with darbepoetin did not reduce either of the composite endpoints,” Marc Pfeffer, MD, PhD (Brigham and Women’s Hospital, Boston) said. “We did observe fewer patients needing red blood cell transfusions and did observe a rather moderate improvement in FACT-fatigue, but we also observed higher rates of stroke.” The observed increase in the risk of thromboembolic episodes is consistent with what has been reported earlier in patients with cancer on ESAs. **These data are very important, and argue against the routine use of ESAs in patients with diabetes, CKD, and anemia.**

N Engl J Med 2009;Oct 30:[Epub ahead of print]

*Adapted from <http://www.cardiosource.com/clinicaltrials/trial.asp?trialID=1880>
<http://www.cardiologytoday.com/view.aspx?rid=50605> as accessed on 17th November 2009*

RE-DEEM: Use of dabigatran with conventional antiplatelet therapy well-tolerated in ACS

Results of Randomized Dabigatran Etexilate Dose Findings Study in Patients With Acute Coronary Syndromes Post Index Event (RE-DEEM) presented at *American Heart Association 2009 Scientific Sessions* revealed that **addition of the oral direct thrombin inhibitor, dabigatran, to conventional antiplatelet therapy was well-tolerated among STEMI and NSTEMI patients.**

The goal of the present study was to compare various dosages of dabigatran with placebo among patients after an acute coronary syndrome. Overall, 1878 stable patients post STEMI or NSTEMI were randomized in RE-DEEM to dabigatran 50 mg twice daily (n = 372), dabigatran 75 mg twice daily (n = 371), dabigatran 110 mg twice daily (n = 411), dabigatran 150 mg twice daily (n = 351), or placebo (n = 373). The mean age of the patients in the study was 62 years, 24% were women, 31% had diabetes, 29% had a previous MI, the index diagnosis was STEMI in 60% and NSTEMI in 40%, 54% had percutaneous coronary intervention (PCI) during their index event, more than 90% were on aspirin and clopidogrel, and the mean time from hospital presentation to randomization was 7.4 days.

At the end of the mean follow-up period of 6 months, **major and clinically significant minor bleeding (by intention-to-treat) occurred in 3.5% of the 50 mg group, 4.3% of the 75 mg group, 7.8% of the 110 mg group, 7.7% of the 150 mg group, and 2.4% with placebo (p < 0.001 for trend). Major bleeding was 0.8%, 0.3%, 2.0%, 1.2%, and 0.5%, respectively.**

The secondary end point i.e. cardiovascular death, MI, or stroke occurred in 4.6%, 4.8%, 3.0%, 3.4%, and 3.8%, respectively.

Serious adverse events were reported in 9% of the 50 mg group, 8% of the 75 mg group, 9% of the 110 mg group, 6% of the 150 mg group, and 9% with placebo. Discontinuation of study treatment was reported in 20%, 16%, 19%, 18%, and 14%, respectively.

Thus, RE-DEEM concluded that **among STEMI or NSTEMI patients, the addition of dabigatran to conventional antiplatelet therapy was well-tolerated. Bleeding was relatively low and it appeared to increase in a dose-dependent manner.** However, further studies are warranted to examine the clinical effectiveness of this agent.

Adapted from <http://www.cardiosource.com/clinicaltrials/trial.asp?trialID=1885> as accessed on 19th November 2009

Analysis of HOPE study: Increased plasma renin activity predicts increased CV events & mortality

Analysis of Heart Outcomes Prevention Evaluation (HOPE) study presented at the *American Heart Association 2009 Scientific Sessions* showed that the **patients with elevated levels of plasma renin activity at baseline were at an increased risk of cardiovascular (CV) death, total mortality, and heart failure.** Thus, the analysis **highlighted the role of renin as a new biomarker of renin angiotensin system (RAS) activation that would help predict CV disease risk.**

Researchers measured the baseline plasma renin activity in 2,913 patients, who had stable vascular disease or diabetes but without heart failure or left ventricular dysfunction, in the Canadian cohort. **The analysis showed that compared with patients in lowest quintile, the patients with increased levels of plasma renin activity i.e. those in the highest quintile, had a significantly increased risk of CV death and total mortality.**

The association between plasma renin activity and CV outcomes persisted after adjustment for multiple variables, including the HOPE score, which accounts for age, sex, hypertension, left ventricular hypertrophy, diabetes, stroke, coronary artery disease, peripheral artery disease, and microalbuminuria, as well as after adjustment for C-reactive protein (CRP) and brain natriuretic peptide (BNP), with a close to a twofold increase in total mortality or CV death (Table 1).

Table 1: Relative risk of CV death and total mortality

Plasma renin activity, ng/mL per hour	Cardiovascular death		Total mortality	
	Adjusted for HOPE score (95% CI)	Adjusted for HOPE score, CRP, and BNP (95% CI)	Adjusted for HOPE score (95% CI)	Adjusted for HOPE score, CRP, and BNP (95% CI)
<0.35	1.0	1.0	1.0	1.0
0.35-0.63	1.58 (0.94-2.64)	1.35 (0.76-2.41)	0.97 (0.67-1.42)	0.84 (0.55-1.26)
0.63-1.03	1.46 (0.87-2.45)	1.60 (0.92-2.81)	0.93 (0.64-1.35)	0.99 (0.67-1.47)
1.03-1.79	1.43 (0.85-2.43)	1.51 (0.85-2.69)	0.94 (0.64-1.37)	0.99 (0.67-1.49)
>1.79	1.75 (1.06-2.90)	1.86 (1.08-3.21)	1.39 (0.98-1.96)	1.43 (1.00-2.06)

The lead investigator of the analysis, Dr Subodh Verma, University of Toronto, ON, further pointed that the **associations were not diluted by assignment to ramipril or to placebo.** Thus, he suggested that **plasma renin activity might be an important biomarker of residual risk in patients who receive conventional RAS blockers.**

Adapted from <http://www.theheart.org/article/1022387.do> as accessed on 17th November 2009

Obese adults may have misperception of body-size

People who are obese may perceive themselves as smaller than actual size - 8% out of 2,056 obese participants stated they were satisfied with their body weight or felt they could gain more weight, according to data from the Dallas Heart study. This was presented by Dr. Tiffany Powell (MD, cardiology, University of Texas Southwestern Medical Center in Dallas) on November 17, 2009 at the *American Heart Association 2009 Scientific Sessions*.

The Dallas Heart study included 5,893 Dallas-county residents classified as below normal weight, normal weight or above normal weight according to the Stunkard Scale. Body weight discrepancy was assessed as the difference between self-perceived actual body weight and ideal body weight.

Those with above normal body weight were more likely to be women (55% vs. 52%; $P<0.0001$), black (72% vs. 56%; $P<0.0001$), had a higher BMI (33 kg m² vs. 28 kg m²; $P<0.0001$), higher systolic BP (130 mmHg vs. 127 mmHg; $P=0.02$) and higher insulin resistance (3.49 units vs. 3.04 units; $P=0.05$) when compared with participants with normal body weight.

Researchers then assessed actual and ideal body weight in 266 obese participants with body-size misperception and 1,790 obese participants without body-size misperception.

Sixty-six percent of obese adults thought they were at low risk for obesity although they were already obese. Further, 44% of obese participants who misperceived their body weight as normal hadn't visited a physician within the previous year vs. 26% of obese participants who knew they needed to lose weight.

Only 38% of those with misperceived body weight discussed dietary changes with their physician compared with 64% of those with more accurate body perception.

Overall results indicated that participants with an above average body weight perceived themselves as smaller than their ideal weight compared with participants with a below normal or normal body weight who perceived themselves as larger than their ideal body weight.

Dr Powel concluded that physicians must understand and target those with body-size misperception in their clinical setting. He also encouraged the development of community-based programs in order to target those with body size misperception who avoided the health care system.

Adapted from www.cardiologytoday.com as accessed on 18th November, 2009

FAIR-HF: Symptom improvement, functional gains follow correction of iron deficiency in heart failure

The intravenous infusion of ferric carboxymaltose in patients with chronic heart failure and iron deficiency leads to improvement in health status, NYHA functional class, six-minute-walk distance and quality of life as per the FAIR-HF study which was presented by Dr Stefan D Anker (MD, cardiologist at Charité Universitätsmedizin, Berlin, Germany) on November 17, 2009 at the *American Heart Association (AHA) 2009 Scientific Sessions* and published online in the *New England Journal of Medicine*.

The iron-replacement therapy benefited the patients regardless of whether they had anemia at baseline suggesting that iron deficiency is a valid independent therapeutic target. The researchers of this study have estimated that about 20% to 30% of ambulatory patients with heart failure have functional iron deficiency.

Researchers for the FAIR-HF trial randomized 459 heart-failure patients who were in NYHA class 2 with an LVEF <40% or NYHA class 3 with an LVEF <45%, had an initial hemoglobin level of 95 g/L to 135 g/L, depressed serum ferritin levels, and no hepatic or renal dysfunction. They were assigned in a 2:1 ratio to receive either ferric carboxymaltose in IV doses each containing 200-mg iron or placebo; dosing was weekly for eight to 12 weeks (depending the patient's calculated iron deficit) and then every four weeks, for a total of 26 weeks of treatment. The primary study endpoint was Patient Global Assessment (PGA) at 24 weeks and NYHA class assessment at 24 weeks. The 304 patients in the iron-repletion group and the 155 controls were similar with respect to heart-failure severity, clinical features, cardiovascular risk factors, laboratory measurements (including those reflecting liver and renal function), and cardiovascular medications.

The researchers reported that PGA at 24 weeks improved in the ferric carboxymaltose group, with 50% of patients reporting either much improved or moderately improved scores vs. 28% in the placebo group (OR=2.51; 95% CI, 1.75-3.61). In addition, NYHA functional class improved in the ferrous carboxymaltose group, with 47% of patients reporting NYHA functional class I or II vs. 30% in the placebo group (OR=2.40; 95% CI, 1.55-3.71). There was also an improvement in six-minute walking distance at four weeks ($P<.001$), 12 weeks ($P<.001$) and 24 weeks ($P<.001$) in the ferric carboxymaltose group. No interactions between secondary endpoints were reported.

Results of six-minute-walk test in meters, ferric carboxymaltose therapy vs placebo

<i>Follow up interval</i>	<i>Iron repletion therapy (m)</i>	<i>Placebo (m)</i>	<i>P value</i>
<i>Baseline</i>	274	269	<i>NS</i>
<i>4 wk</i>	294	269	<i><0.001</i>
<i>12 wk</i>	312	272	<i><0.001</i>
<i>24 wk</i>	313	277	<i><0.001</i>

The benefits of iron therapy for the two primary end points were consistent in all subgroup analyses, including those by sex, age, renal function, NYHA class, LVEF, heart-failure etiology, diabetes status, and body-mass index, and most notably by hemoglobin level (<120 g/L, signifying anemia, vs >120 g/L) and median ferritin level (<39 µg/L vs >39 µg/L).

Dr Stefan Anker said that the treatment was effective in both groups [anemia and no anemia]. There was an increase of hemoglobin of about 1 g/dL in the anemic patients whereas; there was no increase in hemoglobin at all in the nonanemic patients. So the improvement overall in symptoms and self-reported well-being seemed to be related more to the fact that the patient received a correction of iron deficiency rather than a change in hemoglobin by this treatment.

Thus, Dr Anker concluded, “If a patient is symptomatic with HF and has iron deficiency, which is simple to assess, the treatment with intravenous iron should be considered.”

Adapted from www.theheart.org; www.cardiologytoday.com as accessed on 18th November, 2009.

ACC/AHA focused update of guidelines for STEMI, PCI

The American Heart Association (AHA) and the American College of Cardiology (ACC) have issued fast-track updates to the guidance for treatment of ST-elevation MI (STEMI) and for PCI incorporating the latest evidence in these fields. An overview of the guideline updates was presented on November 18, 2009 at the *American Heart Association 2009 Scientific Sessions*.

Chair of the writing group, Dr Sid Smith (University of North Carolina, Chapel Hill) said, "This is the first of a whole new approach with the guidelines, the focused update. What we've done over the past two years is taken key trials presented at major cardiology meetings—the ACC, European Society of Cardiology (ESC), and AHA—that could result in significant improvement or modification in how cardiologists practice and integrated these into the advice. The focused update is a way of responding quickly to new information that will benefit patients."

The following were the updates on guidelines for STEMI and PCI:

Triage and transfer for PCI stressed, but no reference to PCI without surgical backup

The new plan involves protocols for identifying STEMI patients even before they reach the hospital and directing ambulances to centers capable of performing PCI rapidly. For those who initially arrive at hospitals not equipped to perform PCI, the optimal arrangement is for rapid transfer to a PCI center whenever possible. For those who cannot be transferred quickly, fibrinolysis is recommended, and afterward, those judged to be high risk should be transported to a PCI center.

Dr Melissa Walton-Shirley (TJ Samson Community Hospital, Glasgow, KY) believes that specific recommendations should also have been made to encourage the use of PCI hospitals without surgical backup. "In the US, only 4% to 6% of transferred STEMI patients receive PCI within the golden 90-minute time frame, and 20% to 40% of patients have contraindications to lytic therapy," she observes. "Today, my hospital provides more than 80% of STEMI patients with PCI within 90 minutes only because we are participating in a pilot project that allows for PCI without surgery on-site."

"Probably the new recommendation with the greatest impact is that all communities need to look at how they are organized in terms of emergency medical services (EMS) and hospitals, both with and without PCI capability, and how they relate to each other. Institutions also need to set up registries that begin to look at outcomes. This must be done. We are telling people all over the country to come in if you have chest pain, and they are coming in to systems that are not well coordinated," said Smith.

But the Society for Cardiac Angiography and Interventions president and writing committee member Dr Steven R Bailey (University of Texas Health Sciences Center, San Antonio) notes that although this focused update "is rapid, it's still six to nine months ago and antedates a lot of these new trials that are coming out." And while there are "wonderful trials" on this issue, many details remain to be ironed out before any firm recommendations can be made, he says.

More support for stenting the left main, thrombectomy and FFR

Stent-based PCI of the left main coronary artery can be considered as an alternative to CABG in patients with suitable anatomy or in those who are at high surgical risk. Routine surveillance angiography is no longer recommended in patients undergoing left main artery stenting.

Another change is that aspiration thrombectomy is now deemed useful in STEMI patients with short ischemic times and large thrombus burden. Dr Bailey said, "This emerging world of thrombus removal at the time of AMI is practice-changing, and the data—both individual studies and a meta-analysis—all demonstrate that we can further improve upon outcomes in AMI by removing thrombus."

Fractional flow reserve (FFR) can be used to guide need for PCI of a specific coronary lesion and is a useful alternative to noninvasive functional testing in determining the hemodynamic assessment of intermediate coronary stenoses (30-70% luminal narrowing) in patients with anginal symptoms. Routine determination of FFR in patients with angina and a concordant positive, noninvasive functional study is not recommended.

New data on anticoagulants and antiplatelet agents

Bivalirudin can be considered a suitable alternative anticoagulant in patients undergoing primary PCI in STEMI, whether or not the patient received pretreatment with unfractionated heparin. Bivalirudin may be especially valuable in patients at high risk of bleeding.

In patients undergoing primary PCI for STEMI, a loading dose of clopidogrel (300 or 600 mg) or prasugrel (60 mg) should be administered as soon as possible. In patients with STEMI who are treated with a bare-metal or a drug-eluting stent (DES), clopidogrel 75 mg a day or prasugrel 10 mg daily should be continued (if possible) for a year. Continuation of prasugrel or clopidogrel beyond 15 months may be considered in patients treated with DES. In patients treated with clopidogrel, routine use of proton pump inhibitors should be avoided. Prasugrel should be avoided in patients with prior history of stroke or transient ischemic attack.

In patients undergoing primary PCI, it is reasonable to consider use of abciximab or tirofiban or eptifibatide in the catheterization laboratory. The benefit of glycoprotein IIb/IIIa receptor antagonists for patients with STEMI before their arrival in the cardiac catheterization laboratory (upstream use) is uncertain.

Other aspects in PCI for STEMI

In patients with chronic kidney disease undergoing angiography (who are not undergoing chronic dialysis), either an isosmolar contrast medium (Iodixanol) or a low-molecular-weight contrast medium other than ioxaglate or iohexol should be used.

It is reasonable to use an insulin-based regimen to achieve and maintain glucose levels less than 180 mg/dl while avoiding hypoglycemia for patients with STEMI.

Preventing conflict of interest in guideline groups

Dr Sanjay Kaul (Cedars Sinai Medical Center, Los Angeles, CA), who was an official AHA reviewer of the new guidelines, commented, "A recent report from the Institute of Medicine recommends that guideline-writing groups reject all direct industry funding and exclude individuals with any conflicts of interest [COIs]. One way to accomplish the latter goal is to not allow investigators in guideline-relevant trials to participate in related writing committees. It is interesting to observe that while six of 12 members of the writing committee for the STEMI update had no COI, only two of 10 members of the PCI update writing committee reported no COI."

Smith said much effort has been made to try to ensure that the guidelines remain free of bias. Voting was confidential and any members on either committee who had COIs had to recuse themselves and could not vote on an issue where there was a relationship. In addition, says Smith, the power of these guidelines "extends well beyond the people who write them: they have to be reviewed and approved, and these people have to list all their relationships, and that's important." In future, the aim is that only one-third of committee members will have any COIs, says Smith.

Dr Kaul says, "These moves are a step in the right direction. But rather than participate as committee members, such trial investigators should instead act as 'expert witnesses' who can provide advice on and clarifications of the published trial evidence, but not as 'jurors' who compose and/or vote on the guidelines. Only by building a 'firewall' between the guideline-

writing committees and industry or investigator influence will the rigor and integrity of the guideline process be truly enhanced."

But Smith says Kaul's recommendations are impractical: "To write guidelines and not have people who are experienced in clinical trials is very difficult. We actually tried to do that with one guideline a year ago and had to rewrite it. These people were not used to looking at clinical trials and understanding a lot of the issues."

Kaul said this "is a sad reflection on our profession, that we cannot find individuals who do not have financial COIs who are able to provide the kind of expertise that is necessary."

Adapted from www.theheart.org; wwwcardiosource.com as accessed on November 19, 2009

RecordAF Registry: Differences in Clinical Outcomes with Rhythm-and Rate-Control Therapies for Atrial Fibrillation

Results from the **RecordAF registry (REgistry on Cardiac rhythm disORDers assessing the control of Atrial Fibrillation)**, presented on November 15, 2009 at the *Scientific Sessions of the American Heart Association*, show that in recently diagnosed and actively treated patients with atrial fibrillation (AF), a rhythm-control strategy provides better short term control of the arrhythmia versus a rate-control strategy but does not translate into a reduction in the occurrence of clinical events at 1 year.

Atrial fibrillation is a potentially life-threatening disease caused by an erratic electrical activity in the heart which worsens the prognosis of patients with CV risk factors and increases the risk of hospitalization, stroke, and mortality.

RecordAF is the first international prospective, observational survey established to help assess the global burden of atrial fibrillation by investigating the way in which it is managed in "real world" clinical cardiology settings, identifying best clinical practice, and shaping the future management of the disease.

5,604 patients with recently diagnosed atrial fibrillation participated in the RecordAF registry over 12 months, from Apr 2007 to Apr 2008. Co-primary endpoints were therapeutic success and major adverse cardiac events (MACE). MACE was defined as cardiovascular death, myocardial infarction, stroke, transient ischemia attack leading to hospitalization, hospitalization or prolongation of hospitalization (arrhythmic or proarrhythmic events, other cardiovascular events, major complications of ablative procedure) Therapeutic success was defined as either sinus rhythm or controlled rate (depending on strategy) without MACE and without strategy switch.

Rate-control strategy was chosen by treating cardiologists in 45% of patients, rhythm-control strategy in 55%. As expected, rate-control patients were more likely treated with digoxin, calcium-channel blockers, and beta-blockers (excluding sotalol). Rhythm-control patients were more likely treated with antiarrhythmic drugs.

Therapeutic success occurred in 60% and 47% of rhythm-control and rate-control strategy patients, respectively. MACE occurred in 17% and 18% of rhythm-control and rate-control strategy patients, respectively. Multivariate analysis showed that rhythm-control strategy predicted therapeutic success, with an odds ratio of 1.67 (p<0.0001), whereas clinical factors including CAD, heart failure, age > 75, and prior stroke or TIA predicted therapeutic failure. Thus, clinical factors and not treatment strategy predicted MACE.

RecordAF shows that a rhythm control strategy was the preferred therapeutic option (55 percent) at the start of the study. Therapeutic success was 60 percent with a rhythm-control strategy compared to 47 percent with a rate-control strategy. **But, there was no difference in the reduction of clinical events between patients on the rhythm or rate control groups.**

According to Prof John Camm, St George's University, London, UK, joint-lead investigator, RecordAF shows that while a rhythm-control strategy achieves superior therapeutic success in atrial fibrillation than a rate-control strategy, there is no difference in the occurrence of clinical outcomes between strategies and in order to truly optimise the management of atrial fibrillation we need anti-arrhythmic drugs that improve both rhythm- and rate-control and significantly reduce clinical events.

Adapted from www.earthtimes.org; www.cardiosource.com as accessed on 16th November 2009

RAPTOR study: Experienced cardiologists can rapidly shift from femoral-artery to radial-access PCI

Experienced interventional cardiologists can rapidly shift their practice from the femoral-artery to the radial-access approach, with no increase in procedure time and radiation exposure for PCI and with only slight increases in procedure time and radiation exposure for coronary angiography. In addition, the transradial-access technique leads to more economic use of hospital resources, according to researchers. The results of the study were presented by Dr Tim Günter Schäufele (Heart Institute, Germany) during a late-breaking interventional clinical-science session. The session moderator Dr David Cohen (Mid-America Heart Institute) conducted an unscientific poll of the audience following the presentation: a number of individuals acknowledged using the radial-access approach, only two hands remained in the air when he asked how many were in the US.

The **RAPTOR** trial was designed to determine whether operators experienced in femoral access could switch to radial access as a routine strategy in a real-world population and if this switch affected patient safety, radiation exposure, patient comfort, procedural durations, and staff involvement. Over a one-year period, 410 patients at a single, high-volume German center were randomized to femoral- or radial-access intervention, and of these, approximately 75% underwent diagnostic intervention and 25% underwent PCI. In terms of the procedural times, it took significantly more time to puncture the radial artery and to perform coronary angiography, but the procedural time was similar in the femoral-access and radial-access arms in patients undergoing PCI. Radiation times and radiation doses were also higher in coronary-angiography patients treated with the radial-access approach, but there were no differences between the two techniques among patients undergoing PCI. Diagnostic catheterizations and PCI both required more time to compress the access site among patients treated with the conventional femoral approach, roughly 12 minutes, compared with nearly no manual compression time required for patients treated via the radial artery. This led to an overall "time savings" for staff with each procedure, and in a high-volume center performing 3000 procedures annually, including 1000 PCIs, leads to a saving of 1300 hours of staff involvement, said Schäufele.

Dr Alice Jacobs (Boston University, MA) acknowledged the "inertia" among physicians to switch from femoral to radial access, noting that data from the **National Cardiovascular Data Registry** (NCDR) show the approach to be extremely rare in contemporary practice, with just 1.32% of procedures done through the radial artery. Some clinicians are concerned that the technique is slower, especially as they are learning, while others worry about increased radiation exposure. However, she said that increased patient comfort and rapid mobility, not to mention the significant reduction in bleeding complications, with radial-access PCI will likely lead to a shift in clinical practice over time.

Dr Henry Block (Emory University, Atlanta) said the current economic climate for healthcare means that doctors are soon going to have to be responsible for saving money, and the radial-access approach is one way to go. As noted, many leading proponents of the approach, including the RAPTOR investigators, advocate using the radial approach for most patients, rather than as a bailout when femoral access fails.

Adapted from <http://www.theheart.org/article/1021445.do> as accessed on 16th November 2009

EXPIRA: Mechanical aspiration with primary PCI may reduce mortality

Dr Gennaro Sardella (Sapienza University, Rome, Italy) presented the two-year follow-up results from the Thrombectomy with Export Catheter in Infarct-Related Artery During Primary Percutaneous Coronary Intervention (EXPIRA) trial during session on November 15, 2009 at the *American Heart Association 2009 Scientific Sessions*.

The EXPIRA study has shown that the use of a manual thrombectomy device (Export Medtronic; EM) as adjunctive therapy in primary PCI improved procedural outcomes in patients with STEMI. Importantly, this was the first-ever thrombectomy trial to employ contrast-enhanced magnetic resonance imaging (CE-MRI) to assess microvascular damage.

Researchers for the single-center EXPIRA study enrolled 256 patients with STEMI and randomly assigned 175 of them to either thrombectomy plus PCI (n=88) or standard PCI (n=87). The primary study endpoint was a final myocardial blush grade of >3 and ST-segment resolution of more than 70% of the ST segment at 90 minutes. Patients were included if they had STEMI within six to nine hours following symptom onset, had angiographically identifiable occlusive thrombus and a TIMI score of the either zero or one at a time of initial angiography.

At 24 months, 76.3% of patients in the thrombectomy group had a myocardial blush grade of 3, compared with 32% in the conventional-PCI group (p<0.0001) and 80% of the thrombectomy group had at least a 70% decrease in ST segment, compared with 37.5% of the control group (p<0.01).

The EM-PCI group also had fewer adverse events than standard PCI group.

Adverse event	PCI group, n=87 (%)	EM-PCI group, n=88 (%)	Hazard ratio	P value
Cardiac death	6.8	0	6.657	0.0001
Reinfarction	1.1	0	-	0.999
TVR	5.7	4.5	1.302	0.651
MACE	13.6	4.5	3.105	0.050
Very late stent thrombosis	0	0	-	-

TVR=target vessel revascularization
MACE=major adverse cardiac events

Coauthor and imaging specialist Dr Chiara Bucciarelli-Ducci said, "What we wanted to demonstrate was that if we do thrombectomy, then basically the damage at a myocardial level is of a lesser extent than in a patient who did not get thrombectomy. At a tissue level, thrombectomy does make a difference, according to our study, and this is the first time this has been shown."

During a panel discussion, Dr Alice Jacobs (Boston University School of Medicine, MA) commended the EXPIRA investigators for studying a procedure that has already become popular with interventionalists despite limited clinical data to support it. "It's good that we have increasing evidence, because I think that this is one technique where the evidence has really lagged behind clinical practice," she said.

Adapted by www.theheart.org; www.cardiologytoday.com; www.medscape.com as accessed on 16th Nov 2009

PRINCE: Prehospital intranasal cooling after cardiac arrest feasible, may improve survival

Use of a new device that allows therapeutic hypothermia to be instituted in the field at the site of cardiac arrest has been shown to be feasible and safe for patients in cardiac arrest. Results of the Pre-Resuscitation Intranasal Cooling Effectiveness (PRINCE) trial, were presented on November 16, 2009 at the *American Heart Association 2009 Scientific Sessions*.

Therapeutic hypothermia currently is recommended for patients successfully resuscitated from cardiac arrest once they reach the hospital. However, many medical professionals believe that cooling could be more effective if started earlier, ideally at the time of arrest. This study was conducted to determine whether the addition of direct-to-the-brain cooling at the site of cardiac arrest has a beneficial effect.

The PRINCE trial was an attempt to begin therapeutic hypothermia outside the hospital during CPR, using a transnasal system that introduces a mixture of volatile coolant and oxygen into the nasal passages directly under the large vessels of the brain. In the trial, 200 patients who experienced a witnessed cardiac arrest with CPR begun within 20 minutes were randomized to prehospital transnasal cooling or standard advanced cardiac life support (ACLS) care. Cooling was begun as soon as was considered feasible without interfering with ACLS protocols. Patients in both groups received therapeutic hypothermia once they arrived at the hospital. All arrests were included, regardless of the initial rhythm. Of 200 randomized patients, 18 were eventually excluded from the analysis, often because they were later found to have "do-not-resuscitate" orders or other exclusion criteria, leaving 83 in the intranasal-cooling group and 99 in the standard-care group.

The target tympanic temperature of 34°C, used as an approximation of brain temperature, was reached three hours earlier in the group receiving prehospital cooling, and the target core body temperature was reached two hours earlier. Adverse events were minor with nasal discoloration being the most common.

PRINCE: Adverse events with intranasal cooling vs no intranasal cooling

Device-related events	Intranasal cooling (n=83), n (%)	No intranasal cooling (n=99), n (%)
Nasal discoloration	13 (15.6)	0 (0)
Epistaxis	3 (3.6)	0 (0)
Perioral bleed	1 (1.2)	0 (0)
Periorbital emphysema	1 (1.2)	0 (0)
Serious adverse events unrelated to device in admitted patients (sepsis, AMI, rearrest)	6/30 (20)	14/42 (33.3)

31.1% of the standard-care patients admitted to the hospital survived vs 46.7% of those receiving intranasal cooling (p=0.15), not a statistically significant difference. Amongst the 75% of patients who received CPR within 10 minutes of collapse, there was a significant increase in survival, from 29.4% in the standard group to 59.1% in the intranasal-cooling group (p=0.028). Of those with ventricular fibrillation, survival to discharge was not significantly different, at 47.6% in the standard-care group vs 62.5% in the cooled group. Finally, neurologically intact survival was 21.4% with standard care vs 36.7% in those treated with intranasal cooling (p=0.15). Again, significant benefit from cooling was seen in

the subgroup that received CPR within 10 minutes of arrest, with neurologically intact survival rising from 17.6% with standard care to 45.5% with intranasal cooling (p=0.025).

Dr Maaret Castrén (Karolinksa Institute, Stockholm, Sweden) concluded, "Even if the study was not powered for outcome, we can cautiously say that survival and neurologically intact survival to discharge was significantly higher when CPR was initiated within 10 minutes."

Adapted from www.theheart.org; www.dicardiology.net as accessed on 17th November, 2009

French registry study: High Success Rates with Trans-catheter aortic valve implantation

Trans-catheter aortic valve implantation, using either of two commercially available bioprosthetic valves, has almost 100% success in the hands of interventionists trained in this technique, according to results of the first prospective registry to follow high-risk patients undergoing the procedure. “Six-month follow-up data show a high success rate with excellent sustained hemodynamics and clinical improvement, with an acceptable mortality rate in this high-risk population,” stated Helene Eltchaninoff (University of Rouen, France), who presented the results at a late-breaking news session.

The prospective registry included 244 consecutive patients treated at 16 different centers in France. Two-thirds of patients received the Edwards Sapien bioprosthesis, a balloon expandable valve, and one-third received the CoreValve, a self-expandable valve. The Edwards Sapien valve was implanted using either a femoral approach (39%) or an apical approach (29%); the CoreValve was implanted via a femoral approach (27%) or a subclavian approach (5%). The valves come in two different sizes: 23 mm and 26 mm for the Edwards Sapien valve and 26 mm and 29 mm for the CoreValve. Patients included in the registry had severe aortic stenosis, severe symptoms related to aortic stenosis, and were considered as a high surgical risk. Demographic and disease characteristics were similar for both groups: the mean age of participants was 82.3 years, 44% were women, 23% had previous myocardial infarction, 10% had previous stroke, and more than 40% had associated coronary artery disease. Mean left ventricular ejection fraction was 51%. Two thirds of the procedures were performed in the catheter lab, 12.3% in the hybrid room. General anesthesia was used in 84% of cases and trans-esophageal echocardiograph was used in 75% of procedures.

Although Eltchaninoff pointed out that the study was not a randomized, controlled trial designed to compare the two types of valves and should not be interpreted as such, some differences emerged. The contrast volume and x-ray time were longer when a subclavian approach was used to implant the CoreValve. Success and failure rates were comparable for the two different valves. Complication rates were also similar between these two groups, with the exception of a **significantly greater percentage of patients implanted with the CoreValve requiring a new pacemaker after the procedure: 27% versus 4.2% for the Edwards Sapien valve (p<0.001). For the whole group, 30-day mortality was 12.7%, cardiac tamponade occurred in 2%, stroke was reported in 3.6%, and coronary occlusion in 1.2%.** Six-month follow-up data were available for 111 patients (76.5%). Of these, 86% were New York Heart Association (NYHA) functional class 1 or 2, even though all patients were NYHA>2 prior to having the trans-catheter procedure. Six-month follow-up of the rest of the patients is ongoing, Eltchaninoff said, “but so far, survival appears to be similar to previously reported series.”

Trans-catheter aortic valve implantation was first introduced in 2002 as an alternative to conventional aortic valve implantation. In 2009, more than 10,000 patients worldwide were treated with this technique. According to panelists who commented on the study, the 97% success rate shown by registry data was remarkable and suggested that the learning curve phase for this intervention was over. A total of seven failed procedures occurred, including four procedural deaths.

Adapted from http://www.incirculation.net/aha09/18471_108475.aspx as accessed on 16th November 2009

REPLACE registry: Fifteen % six-month complication rate with pacemaker and ICD lead replacements

Dr Jeanne Poole (University of Washington, Seattle) presented the data from REPLACE on complications with planned lead upgrades or additions during a late breaking clinical-science session on November 16, 2009 at the *American Heart Association 2009 Scientific Sessions*.

The REPLACE registry enrolled 1000 patients undergoing ICD or pacemaker replacement only and 750 patients undergoing lead additions or revisions. Complications were predefined and adjudicated by a core events committee. **The overall rate of minor events, such as hematoma, blistering, or reprogramming for changed status was 7.6%, affecting 54 patients. Major perioperative (within 24 hours) complications, including cardiac perforation and hemothorax, affected 17 patients, for a rate of 2.4%. A total of 100 patients had at least one major complication within six months of the procedure, for a rate of 14%. The most common major event was malfunction requiring reopening of the pocket (46 patients, 6.5%). Also, 26 patients (3.7%) had an unplanned lead removal or addition. There were eight deaths (1.1%).**

Rate of any major complication by type of lead procedure

Procedure	Patients with complication	Rate (%)
LV lead addition or revision (n=434)	81	18.7
RA/RV lead addition or revision (n=234)	26	11.1
No lead addition or revision (n=45)	2	4.4

Discussing the REPLACE data, Dr Alan Kadish (Northwestern University Medical School, Chicago, IL) said, "The risk/benefit ratio of lead addition needs careful evaluation. Particularly in patients where an atrial lead is added for soft indications, we need to be careful that we think about the risk. LV lead addition is still quite reasonable for overt CHF, but prophylactic addition of LV lead simply because we have a class II patient with battery depletion is something that ought to be carefully thought about in light of the results of the study."

Adapted from www.theheart.org as accessed on 17th November, 2009

Secondary findings of FOCUS: Symptom-based strategy best in terms of blood transfusion for elderly patients post hip surgery

Findings of a randomized trial in patients who underwent surgery for hip-fracture repair suggested that **elderly people with heart disease or major cardiovascular (CV) risk factors needn't automatically receive transfusions if their hemoglobin drops moderately after major surgery, at least if the goal is to prevent CV events.**

Transfusion Trigger Trial for Functional Outcomes in Cardiovascular Patients Undergoing Surgical Hip Fracture Repair (FOCUS), presented at the *American Heart Association 2009 Scientific Sessions*, randomized 2016 patients (mean age 81 yrs, 75% women) with heart disease or major CV risk factors undergoing surgery for hip repair at 47 centers in North America to one of the two transfusion strategies:

- Aggressive or liberal approach, where transfusion was done when hemoglobin drops below 10 g/dL, with enough blood to keep hemoglobin above that threshold; or
- Conservative or restrictive strategy, in which blood was given on development of symptoms or at the physician's discretion or on hemoglobin falling to <8 g/dL

Patients with CAD, heart failure, peripheral vascular disease, stroke or transient ischemic attack, diabetes, hypertension, dyslipidemia, or chronic renal insufficiency were included in the study. Prevalence of these conditions were similar in the two randomization groups.

Of the patients in the aggressive-management group, 97% received transfusions vs 41.5% in the conservative-management group. In the latter group, 2/3rd received blood because their hemoglobin went to <8 g/dL. As a whole, the conservative-management group received about 1/3rd as much blood (652 units) as the aggressive-management group (1866 units).

Most importantly, there was no significant difference in in-hospital mortality rates of myocardial infarction (MI), death, cardiac death, or a composite of MI, unstable angina, or death between the two groups (Table 1).

Table 1: Incidence of in-hospital events

End point	Aggressive strategy (10 g/dL threshold), n=1005 (%)	Conservative strategy (symptom driven), n=1008 (%)
Isolated troponin elevation	6.2	5.9
In-hospital mortality	2.0	1.4
MI, unstable angina, or death	4.3	5.2

Post the trial result presentation, the discussant, Dr Paul W Armstrong, University of Alberta, Edmonton, pointed towards some issues regarding FOCUS. The intervention was open-label and the number of participants fell short of the originally planned sample of 2600 patients. To enhance enrollment, the protocol had been modified after the trial started to allow entry of patients with CV risk factors, whereas previously it had been restricted to patients with manifest CV disease. These limitations, according to him, could weaken trial results.

However, both Dr Paul W Armstrong & the trial investigator, Dr Jeffrey L Carson, University of Medicine and Dentistry of New Jersey, New Brunswick, said that on basis of the trial, symptom-based strategy is best for patients who undergo hip-surgery i.e. **follow the patients, don't transfuse on a number, but individually assess them, and if they don't have symptoms, it might be reasonable to withhold blood at least down to an 8 g/dL threshold.**

CT-STAT study: CT angiography faster and less expensive than standard diagnostic testing in CAD

The use of coronary computed tomography (CT) angiography in the emergency room can successfully triage at-risk chest-pain patients and can do so faster and less expensively than standard diagnostic testing, according to the results of Computed Tomographic Angiography for the Systematic Triage of Acute Chest Pain Patients to Treatment (CT-STAT) trial presented at the late-breaking clinical-trials session at the *American Heart Association Scientific Sessions*. **Although the use of CT to rule out coronary artery disease should not be used in all patients, especially those with manifest ischemia, electrocardiogram abnormalities, or elevations in enzymatic biomarkers, among low-risk patients, "wisely and prudently applied," CT angiography is a powerful addition to the armamentarium of clinicians**, said lead investigator Dr James Goldstein (William Beaumont Hospital, MI).

Dr Kavitha Chinnaiyan (William Beaumont Hospital), a co-principal investigator, said that more than six million visits to the emergency department for chest pain occur in the US each year. Although estimates vary, she said that MI is missed in 4% to 13% of patients, and of these patients, mortality rates range from 10% to 25%. These missed MIs result in "huge litigation dollars," said Chinnaiyan, and account for 20% of all emergency-department malpractice dollars spent. In addition, she said that **while standard diagnostic care, which consists of serial electrocardiograms (ECGs) and the measurement of cardiac enzymes taken at baseline and eight to 12 hours after presentation, coupled with rest and/or myocardial perfusion imaging, reduces diagnostic errors, the process is time-consuming and resource intensive**. "The longer you spend in the hospital, the more money is spent, and it's not always definitive," she said.

In CT-STAT, investigators included 750 patients with chest pain in the past 12 hours who presented to the emergency department and who had normal ECG and cardiac enzymes. These patients were randomized to a standard diagnostic workup or to the CT-angiography arm. Among the CT-treated patients, those with severe stenosis, >70%, were taken immediately to the catheterization lab for invasive angiography, while those with intermediate stenosis or uninterpretable CT images were sent for a nuclear stress test. An abnormal stress test resulted in invasive angiography, while patients with a normal result were sent home.

In the CT-angiography arm, there was no significant stenosis detected in 82.3% of patients, leading to an immediate discharge of 190 of 262 patients. At least one significant stenosis (>50%) was detected in 7.5% of CT patients, and moderate stenosis (25% to 50%) was detected in 9% of patients. Among those undergoing conventional care, myocardial perfusion imaging was normal in 90% of patients. **Both CT angiography and conventional care led to similar number of patients referred for invasive coronary angiography, 6.9% and 6.2%, respectively. Regarding the primary outcome, the time to diagnosis and hospital costs were significantly reduced with CT angiography. CT patients were discharged in approximately three hours compared with seven hours for those who received standard care. The costs were reduced 38% among those treated with CT, reduced from roughly \$3500 with standard care to \$2000 for CT angiography.**

Commenting on the study, Dr John Hodgson (Geisinger Heart Institute, PA), past president of the **Society of Cardiovascular Angiography and Interventions (SCAI)**, said that **no imaging test is as good as coronary CT angiography for ruling out coronary artery disease, with some studies reporting negative predictive accuracies of 99%. Myocardial perfusion imaging, on the other hand, has good prognostic value but is not nearly as good at ruling out disease**. As a result, there are increased false positives—an abnormal stress test result but no clinical disease—and this sends the patient for more and more tests, increasing the costs to the hospital.

Dr Robert Bonow (Northwestern University Feinberg School of Medicine, Chicago), a discussant, called **CT-STAT an excellent study, one that needs to be done for imaging, because it studies a strategy that can be implemented in the processes of care.** Although he praised the results, he questioned whether the same findings could be reproduced by a less experienced center. In addition, he raised concerns about radiation exposure, especially if clinicians use CT to rule out other cardiac-related problems. Hodgson, however, told that the radiation issue for CT angiography has been "overblown." He said that nuclear stress testing provides a radiation exposure of 15 mSv, even more if thallium is used, but the newer CT protocols and improved technology provides only 3 mSv.

Adapted from <http://www.theheart.org/article/1026349.do> as accessed on November 19th, 2009

PEPCAD-3 study: Paclitaxel-coated-balloon/stent system not up to the mark of the Sirolimus-eluting stent

In a third trial in the **Paclitaxel-Eluting PTCA-Balloon Catheter in Coronary Artery Disease series (PEPCAD 3)**, a PCI system consisting of a balloon coated with paclitaxel paired with a bare-metal stent didn't measure up to the Cypher stent (sirolimus-eluting stent, Cordis/Johnson & Johnson) at nine-month angiography. Late in-stent lumen loss after the novel procedure was significantly and markedly greater, and its associated target-lesion- and target-vessel-revascularization (TLR and TVR) rates were double those from Cypher stenting. This study was conducted in six European countries and the first major test of the coated-balloon/bare-metal-stent system.

The 637 patients in the PEPCAD-3 intention-to-treat analysis, who had stable or unstable angina or documented ischemia (STEMI and NSTEMI excluded), were randomized to undergo PCI with either the paclitaxel drug-eluting-balloon/bare-metal-stent system (n=312) or the sirolimus DES (n=325). For each patient, the preprocedure intention had to be treatment of one de novo lesion in a native coronary artery considered manageable with one stent; the stenosis could be >2.5 mm to <3.5 mm in diameter and <24 mm in length. Of the randomized patients, 609 were included in the nine-month follow-up overall, and 542 in the per-protocol nine-month angiographic analysis for the primary outcome.

Late loss at nine months by quantitative coronary angiography: primary analysis

Angiographic end points	Paclitaxel-eluting balloon/bare-metal stent, n=269	Sirolimus-eluting stent, n=273	p
In-stent late loss (mm)	0.41	0.16	<0.001
In-segment late loss (mm)	0.20	0.11	0.06

TVR and TLR rates* at nine months: secondary analysis

Secondary end points	Paclitaxel-eluting balloon/bare-metal stent (%)	Sirolimus-eluting stent (%)	p
TVR	13.8	6.9	<0.01
TLR	10.5	4.7	<0.01

*By intention to treat

Of the safety end points, the rate of MI at nine months was 4.6% and 0.3% (p<0.001) in the drug-eluting-balloon/bare-metal-stent and DES groups, respectively. Also, stent thrombosis by Academic Research Consortium (ARC) criteria was 2.0% and 0.3%, respectively (p<0.05).

Dr Christian Hamm (Kerckhoff Heart Center, Germany) noted, however, **that the device's performance for the late-lumen-loss primary end point was "comparable to published data on paclitaxel-eluting stents."** He said they were taken off guard by the coated-balloon/bare-metal-stent system's failure to show at least parity with the Cypher, based on animal data and earlier clinical studies. He said he can't tell whether that was by chance or for some undetermined reason: patients in the two groups were consistently similar at baseline, for the most part, and the procedural characteristics of stent implantation went about the same, too. The exceptions were stent inflation pressure, which was slightly but significantly lower in the coated-balloon group (14.1 bar vs 14.6 bar, p<0.01) and duration of inflation, which was significantly longer in that group (51.9 s vs 25.0 s, p<0.0001). "The balloon inflation was doubled, and that may have contributed to a higher restenosis risk, but we'll have to explore this further, and we will in every patient," he said.

Referred to as a drug-eluting balloon despite its fairly rapid drug delivery—virtually the entire drug coating is transferred to the vessel wall during one prolonged balloon inflation—the paclitaxel-coated balloon can deliver up to three times the drug dose of a conventional drug-eluting stent (DES), Hamm said. In prior tests of the device, when it was used without follow-up

stenting, the drug-eluting balloon surpassed quaint, uncoated angioplasty balloons and modern DES, the paclitaxel-eluting Taxus (Boston Scientific) in particular, for angiographic outcomes at six months.

For the current study, inflation of the paclitaxel-coated balloon was followed by deployment of a cobalt-chromium bare-metal stent, the Coroflex DEBlue (B Braun Melsungen). "The advantage of a drug-eluting balloon," Hamm said, "would be that you'd need **clopidogrel** for only four weeks—because in two or three days [after the procedure], all you have is a bare-metal stent, with all the advantages of bare metal over a drug-eluting stent, in terms of late thrombosis and all the rest."

Discussant Dr Peter Block (Emory University, Atlanta) lauded the idea that a balloon could deliver a drug into the vessel wall without the need to leave a stent in place. That was the very strategy explored in previous studies of this particular drug-eluting balloon, he observed. Following drug-eluting-balloon inflation with delivery of a bare-metal stent, therefore, conceivably takes away a key drug-eluting-balloon advantage, that it doesn't permanently implant a piece of metal, Block said. The PEPCAD investigators "probably thought that the drug-eluting balloon would overcome the increased TVR and TLR that the bare-metal stent produces, but they failed on that one."

Adapted from <http://www.theheart.org/article/1021669.do> as accessed on 16th November 2009

Platelet function assays help predict risk of adverse outcomes after PCI: POPULAR study

Three tests of platelet reactivity were able to predict which patients undergoing an elective percutaneous coronary intervention (PCI) would have a thrombotic event within one year, despite antiplatelet therapy, researchers reported at the *American Heart Association Scientific Sessions 2009*.

Up to 36% of patients are resistant to clopidogrel, which increases the risk for thrombotic complications following PCI. The issue remains relevant even after the introduction of the more potent antiplatelet prasugrel, because there is still some variability in on-treatment platelet reactivity, albeit less than with clopidogrel.

Guidelines from the American College of Cardiology, American Heart Association, and Society for Catheterization and Angiography recommend platelet function testing in high-risk patients undergoing PCI, but do not recommend a specific method. If inhibition of platelet aggregation is less than 50%, the guidelines state, clinicians may consider increasing the clopidogrel dose.

However, it is unclear which platelet function best predicts clinical events. Hence the POPULAR (Do Point-of-Care Platelet Function Assays Predict Clinical Outcomes in Clopidogrel Pretreated Patients Undergoing Elective PCI) study was conducted by Jurrien M ten Berg and colleagues to assess which of the several available assays is best for predicting risk of thrombotic events.

In the study, ten Berg and his colleagues compared the predictive ability of six tests -- five commercially available and one investigational -- in 1,069 patients undergoing elective PCI with stent placement. All received aspirin and clopidogrel. The researchers assessed the occurrence of a composite of all-cause death, acute myocardial infarction, ischemic stroke, and stent thrombosis through one year. The one-year primary safety endpoint was TIMI major and minor bleeding. The six tests evaluated were: light transmittance aggregometry (LTA) (5 & 20 $\mu\text{mol/L}$ ADP), VerifyNow[®] P2Y12, Plateletworks[®], IMPACT-R, IMPACT-R ADP, PFA-100 COL/ADP, and INNOVANCE[®] PFA P2Y.

High platelet reactivity on three tests significantly predicted adverse outcomes compared with patients who had normal reactivity:

- **Light transmittance aggregometry** using 5 $\mu\text{mol/L}$ adenosine diphosphate (ADP): 11.7% versus 6% ($P < 0.0001$)
- **Light transmittance aggregometry** using 20 $\mu\text{mol/L}$ ADP: 12% versus 6.2% ($P < 0.0001$)
- **VerifyNow P2Y12 assay**: 13.3% versus 5.7% ($P < 0.0001$)
- **Plateletworks assay**: 12.6% versus 6.7% ($P = 0.002$)

According to ten Berg, light transmittance aggregometry is the most labor intensive of the tests and can't be performed at the bedside. Plateletworks is limited in that it must be performed within 10 minutes of drawing blood. **VerifyNow, on the other hand, is fully automated and can be performed in the cath lab**, he said.

The three other tests -- IMPACT-R, PFA-100 with the Dade PFA Collagen/ADP Test Cartridge, and the investigational INNOVANCE PFA P2Y -- did not predict risk. None of the six tests predicted the risk of bleeding complications.

Large randomized trials are underway to assess whether the tests can help clinicians adjust therapy in patients with hyperreactive platelets to improve clinical outcomes, ten Berg said at a press briefing at the American Heart Association meeting.

Adapted from: www.medpagetoday.com; www.cardiosource.com as accessed on 16th November 2009