

Population Trends in the Incidence and Outcomes of Acute Myocardial Infarction.

Yeh RW, Sidney S, et al:

N Engl J Med 2010; 362 (June 10): 2155-2165

Although the use of troponins initially (artificially) increases the incidence of non–ST-elevation type myocardial infarction, rates in recent years are declining.

**Background:** Much progress has been made in recent decades in primary and secondary prevention of acute myocardial infarction (MI). However, the resultant treatments have generally not been tested in large, diverse, unselected populations.

**Objective:** To assess the effects of current treatment on the incidence, severity, and short-term mortality of MI in a large, diverse, community-based cohort.

Methods: Using the Kaiser Permanente Northern California database (covering 3 million people), hospitalizations for acute MI among those aged ≥30 years were identified for the period 1999-2008. MIs were classified as ST-elevation type MI (STEMI) or non–ST-elevation type MI (NSTEMI) based on discharge diagnoses. Data were collected on the MB fraction of creatine kinase (CK-MB) levels, patient demographics, pre-admission medications, revascularization procedures, and 30-day case fatality rates.

**Results:** 46,086 hospitalizations for incident MI were identified, one third with STEMI and two thirds with NSTEMI. From 1999-2008, the proportion of MIs that were STEMIs declined from 47.0% to 22.9%. The ageand sex-adjusted incidence of MI increased from 1999-2000 (274 to 287 per 100,000 person-years), then decreased yearly, reaching 208 per 100,000 person-years in 2008. During the study, STEMI rates decreased yearly, with a total decline of 62% (P <0.001 for trend). The NSTEMI incidence increased from 1999-2004 and decreased thereafter. Over the course of the study, patients were older, were more often female, had more comorbidities, and had more prior revascularization procedures. At the same time, the use of statins, betablockers, and angiotensin-converting-enzyme inhibitors/angiotensin II-receptor blockers increased. During this time, peak CK-MB levels decreased among MIs overall and NSTEMI in particular; there was no trend among STEMI patients. Revascularization within 30 days increased in both types of MI (40.7% to 47.2%; P <0.001 for trend for all MIs), while 30-day mortality for all MIs decreased (10.5% to 7.8%; P <0.001 for trend); the latter was driven by decreased mortality in NSTEMI with little change in mortality for STEMI.

**Conclusions:** From 1999-2008, the incidence of MI decreased, as did case fatality rates; this occurred despite documented increases in such risk factors as obesity and diabetes. Paralleling this were increases in the use of effective medications, improvement in lipid levels and blood pressure control, and decreases in cigarette smoking. A new definition of MI and the increasing use of troponins over this period resulted in an initial increase in NSTEMI; however, after 2004 (when troponin usage was widespread), NSTEMI rates decreased, likely reflecting a true decline in incidence.

**Reviewer's Comments:** This was a carefully done study in a very large population. Drawbacks include a heavy reliance on discharge coding, assumptions about the stability of the covered population, and the use of multiple, complex statistical manipulations. However, these limitations are unlikely to materially affect the results. The key strength of this research is its population-based nature; it is inherently more accurate to study the entire population of interest than a selected sample. (Reviewer-Gregg S. Pressman, MD).

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Keywords: Population Trends, Acute Myocardial Infarction, Treatment

# **PVC-Induced Cardiomyopathy -- Prompt Attention Needed**

Relationship Between Burden of Premature Ventricular Complexes and Left Ventricular Function.

Baman TS, Lange DC, et al:

Heart Rhythm 2010; 7 (July): 865-869

Patients with frequent premature ventricular contractions (PVC) and left ventricular dysfunction should receive prompt treatment to reduce the daily PVC burden.

**Background:** Patients with frequent premature ventricular contractions (PVCs), in the absence of ischemic heart disease, are at risk for developing left ventricular (LV) dysfunction. Not all patients with frequent PVCs develop LV dysfunction, and it is unknown what daily burden of PVCs is associated with developing such dysfunction.

**Objective:** To identify a numerical cut-off of daily PVC burden resulting in LV dysfunction.

**Methods:** Retrospective analysis of data from 174 patients referred for ablation of frequent PVCs. The mean age was 48 years, and the mean LV ejection fraction (EF) was 51%. The group included 87 women. Most patients experienced palpitations, and 11 presented with heart failure symptoms. Echocardiographic evidence of LV dysfunction was present in 57 patients (mean LVEF, 35%). All patients had failed at least one anti-arrhythmic drug. Coronary disease was ruled out. Echocardiography was performed at baseline and was repeated 3 to 4 months after ablation in those with initial evidence of LV dysfunction. An LVEF <50% was considered abnormal. The daily PVC burden was assessed with Holter monitoring at baseline and 3 to 6 months after ablation. Electrophysiology studies were performed in all patients, and the foci responsible for the PVCs were localized and ablated with radiofrequency energy. The procedure was deemed successful if the daily PVC burden was reduced by >80%. Reversal of cardiomyopathy required normalization of LVEF to >50% or an absolute increase by >15% from baseline. Clinical follow-up lasted 3 to 48 months. Anti-arrhythmic drugs were stopped after a successful ablation procedure unless needed for other reasons.

**Results:** Age was similar between the cardiomyopathy and no-cardiomyopathy groups, but the cardiomyopathy group included more males. Multivariate analysis failed to show male gender as an independent risk factor for developing cardiomyopathy. The overall PVC burden at baseline was 20% ± 16%. PVCs were monomorphic in 135 patients and pleomorphic in 39 others. LV dysfunction was clearly associated with a higher burden of PVCs (HR, 1.12). A daily PVC burden of 24% was associated with the best sensitivity/specificity combination to predict LV dysfunction (sensitivity, 79%; specificity, 78%). Some patients above that cut-off point did not develop LV dysfunction, and some with a daily PVC burden as low as 10% developed reversible cardiomyopathy. Ablation was successful acutely and on long-term follow-up in reducing PVC burden by at least 80% in >80% of patients. Among those with LV dysfunction, 81% had significant improvement in LV function after a mean of 3.6 months.

**Conclusions:** A PVC burden of >24% is statistically associated with developing LV dysfunction with a sensitivity and specificity of 80%.

**Reviewer's Comments:** PVC-induced cardiomyopathy is a real entity. The presence of unexplained cardiomyopathy in a patient with frequent PVCs should prompt measures (pharmacologic or invasive) to reduce the PVC burden, and then the response should be re-assessed. (Reviewer-Khalid Almuti, MD).

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Keywords: Premature Ventricular Contractions, Cardiomyopathy

# **Creatine Supplementation Does Not Improve Outcome in Cardiac Rehabilitation**

Effect of Creatine Supplementation as a Potential Adjuvant Therapy to Exercise Training in Cardiac Patients: A Randomized Controlled Trial.

Cornelissen VA, Defoor JGM, et al:

Clin Rehabil 2010; June 24 (): epub ahead of print

The marked improvements in cardiopulmonary performance measures, muscle strength, and quality of life that result from cardiac rehabilitation are not augmented by the addition of oral creatine supplementation.

**Background:** Reduced aerobic capacity and muscle weakness in patients with coronary artery disease (CAD) and congestive heart failure (CHF) are associated with increased morbidity and mortality. Exercise training in cardiac rehabilitation (CR) results in increases in aerobic capacity and muscle strength, as well as reductions in symptoms and improvements in overall functional status. Oral creatine supplementation enhances muscle strength and the effect of physical training in healthy adults. The effect of creatine supplementation on the results of a CR program has not been investigated.

**Objective:** To examine the effect of CR plus oral creatine supplementation on physical fitness in CAD and CHF patients.

**Design:** Single-center, double-blind, randomized, placebo-controlled trial.

**Participants:** 70 patients (66 males, 4 females; age,  $57.5 \pm 8.4$  years) with CAD or CHF; 37 patients were in the placebo group, and 33 were in the creatine group.

**Methods:** All patients were enrolled in a 3-month CR program. They exercised 3 times weekly for 90 minutes per session. Each session consisted of endurance training, moderate resistance training, and relaxation. Each participant ingested 9 g of a water-soluble powder daily (placebo or 5 g of creatine). Patients were evaluated at baseline and after 3 months regarding the following: maximal graded bicycle test, health-related quality-of-life questionnaire, resting left ventricular ejection fraction, muscle performance, fasting blood samples (including lipid profile), and 24-hour urine collection (including urinary creatine excretion).

**Results:** Baseline characteristics of the creatine and placebo groups were the same except that the placebo patients were older (59.7 ± 6.7 vs 55.0 ± 9.5 years; P = 0.02). All cardiopulmonary performance measures, parameters of muscle function, and aspects of health-related quality of life significantly improved after CR in all patients. There were no differences between groups (interaction effect, all P > 0.40). Blood and urine tests were normal and unchanged in both groups, with the exception of a significant drop in HDL and triglycerides in all patients and an increase in urinary creatine excretion in the creatine group only. No adverse effects were reported.

**Conclusions:** Creatine supplementation during a 3-month CR program does not confer additional improvement in health-related quality of life, physical performance, or lipid profiles in patients with CAD and CHF over exercise training alone.

**Reviewer's Comments:** The results of the study show that taking oral creatine at a rate that improves the results of exercise training in healthy subjects is safe but does not enhance the benefits of CR in patients with CAD or CHF. It is possible that any benefit of creatine supplementation in this study may have been eclipsed by the larger effect of the exercise training intervention alone. Perhaps adding creatine after CR is concluded might help these patients improve further. Future studies in this area are needed. (Reviewer-Debra L. Braverman, MD).

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Keywords: Cardiac Rehabilitation, Creatine Supplementation



Usefulness of Exercise-Stress Echocardiography for Risk Stratification of True Asymptomatic Patients With Aortic Valve Stenosis.

Maréchaux S, Hachicha Z, et al:

Eur Heart J 2010; 31 (June): 1390-1397

Exercise-stress echocardiography may help risk stratify asymptomatic aortic stenosis.

**Background:** Management of patients with asymptomatic moderate or severe aortic stenosis (AS) is not well defined. There is concern that moderate asymptomatic AS may progress rapidly, with unclear evidence for optimal follow-up intervals. An abnormal exercise test is defined as the presence of exercise-limiting symptoms, a decrease in blood pressure below baseline, or complex ventricular arrhythmias. Its prognostic benefit is well established in predicting clinical events in asymptomatic patients with AS.

**Objective:** To determine whether exercise-stress echocardiography (ESE) adds incremental prognostic information to resting echocardiography in patients with AS who have a normal exercise response. The mean follow-up was  $20 \pm 14$  months.

**Methods:** Doppler-echocardiographic and clinical data were prospectively collected in 186 patients. These patients were asymptomatic with at least moderate AS and preserved left ventricular (LV) ejection fraction ( $\geq$ 50%). Doppler-echocardiography was performed at rest and during a maximum ramp semi-supine bicycle exercise test. Fifty-one patients had an abnormal exercise test and were excluded from the study analysis. In the 135 patients with a normal exercise test, 67 had an event including aortic valve replacement motivated by symptoms or cardiovascular death. Statistically significant variables independently associated with events were age  $\geq$ 65 years, diabetes, LV hypertrophy, resting mean gradient >35 mm Hg (P <0.0001), and exercise-induced increase in mean gradient >20 mm Hg (P <0.0001).

**Conclusions:** In patients with a normal exercise response, an increased exercise-induced transvalvular gradient may provide incremental prognostic value in asymptomatic patients with AS.

**Reviewer's Comments:** This study illustrates the incremental prognostic value of ESE in patients with asymptomatic AS who have a normal exercise test. The study importantly included patients with at least moderate aortic stenosis. Moderate aortic stenosis, even when completely asymptomatic, may not be a benign entity. Progression to a more severe stage of aortic stenosis may be rapid. This is a heterogenous group, with some patients being symptom free for many years and some rapidly progressing to left ventricular dysfunction. There are, however, no clear data on the optimal follow-up intervals when monitoring these patients (6, 12, or 24 months) and the optimal timing for aortic valve replacement. This study reveals that, in patients with at least moderate AS who are truly asymptomatic (ie, do not have an abnormal exercise-stress test), a significant increase in exercise gradient may help identify patients who are at higher risk for rapid progression of disease. This progression usually results in valve replacement due to worsening symptoms or cardiovascular death. ESE may, therefore, provide additional prognostic information compared to standard exercise testing and resting echocardiography. Patients with a resting mean gradient >35 mm Hg and an exercise-induced increase in gradient >20 mm Hg may require follow-up every 6 months. (Reviewer-Suraj Maraj, MD).

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Keywords: Asymptomatic, Aortic Valve, Stenosis, Exercise-Stress Echocardiography

# **Understanding Bicuspid Aortic Valve Disease**

Bicuspid Aortic Valve Disease. Siu SC, Silversides CK:

J Am Coll Cardiol 2010; 55 (June 22): 2789-2800

Bicuspid aortic valve is an aortic disease, and evaluation of the thoracic aorta is as important as evaluation of the valve.

Background: Bicuspid aortic valve (BAV) is the most common congenital cardiac defect (prevalence, 0.5% to 2%). The most common pattern is fusion of the right and left coronary cusps. This pattern is associated with coarctation of the aorta. The most common associated abnormality is dilatation of the ascending aorta. This is partly due to post-stenotic dilation, but cellular derangements in the aortic wall (including decreased fibrillin, elastin fragmentation, and apoptosis) are seen. These changes are also present, to some extent, in the pulmonary artery. BAV can be associated with coarctation of the aorta (50% to 75% of patients with coarctation will have BAV), Shone's syndrome (multiple left-sided obstructive lesions), Williams syndrome (supravalvular aortic stenosis), Turner syndrome, ventricular septal defect, patent ductus arteriosus, atrial septal defects, cervicocephalic aneurysms, and intracranial aneurysms. **Diagnosis:** Although multiple gene mutations are thought to cause BAV, currently, genetic screening is not clinically useful. There is a 9% prevalence of BAV among first-degree relatives. Thus, echocardiographic screening of first-degree relatives is important. The imaging features include asymmetric closure of the valve, systolic doming, and fish-mouth opening in systole. Since most BAVs will have a raphe, the valve can appear tri-leaflet in diastole on the basal short axis view by echocardiography: therefore, the evaluation should be made in systole, in which the fish-mouth opening can be appreciated. Symptoms typically develop in adulthood and are due to the predominant valve lesion (stenosis or rarely severe regurgitation), dissection, or endocarditis. The valves calcify due to shear stress by the age of 40 years. Prognosis: Patients with no significant valve disease have a 90% survival at 20 years, and those with a spectrum of valve dysfunction have 96% survival at 10 years. This is comparable to the life expectancy of the general population. The predictors of adverse events are age and the severity of valve dysfunction. Those with aortic root >40 mm need annual cardiac imaging with complete imaging of the thoracic aorta done periodically. An aortic sinus dimension of 2.1 cm/m2 is considered the upper limit of normal. Blood pressure should be controlled, and beta-blockers have a class IIa recommendation. Endocarditis prophylaxis is no longer recommended. Indications for surgery are similar to those for tricuspid aortic valve disease. An aortic root size of >50 mm merits root replacement, as does a size of >45 mm if surgery is otherwise being done for valve indications. Although overall mortality in pregnant women with severe BAV stenosis is only 1%, those with root dilation >45 mm should be counseled against pregnancy. Those with severe aortic stenosis or severe regurgitation with ventricular dilation or root >45 mm should avoid competitive sports. Reviewer's Comments: This excellent state-of-the-art paper summarizes our current understanding of BAV

disease and provides useful pointers for our daily clinical practice. (Reviewer-Anoop C. Parameswaran, MD).

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Keywords: Bicuspid Aortic Valve, Outcomes, Review

### Visible Collaterals Associated With Lower Risk Post-MI

Impact of Collateral Flow to the Occluded Infarct-Related Artery on Clinical Outcomes in Patients With Recent Myocardial Infarction: A Report From the Randomized Occluded Artery Trial.

Steg PG, Kerner A, et al:

Circulation 2010; 121 (June 29): 2724-2732

In the setting of acute myocardial infarction, visible collaterals appear to be protective.

**Background:** Visible collaterals are thought to protect patients during acute myocardial infarction (MI). However, their impact on outcomes in patients undergoing primary percutaneous coronary intervention (PCI) is controversial.

**Design:** The Occluded Artery Trial (OAT) randomized 2201 patients (3 to 28 days post-MI with an occluded infarct-related artery) to either PCI plus medical therapy or medical therapy alone (MED). The primary outcome was a composite of all-cause mortality, reinfarction, and class IV heart failure (HF), with no significant benefit of PCI found in the main trial. The current research examined the influence of angiographically visible collaterals on this outcome.

**Methods/Results:** Core laboratory data on collateral flow were available on 1087 PCI patients and 1086 MED patients. Distribution of collaterals was similar in the 2 groups. Overall, those with higher collateral flow had lower baseline risk profiles (younger age, fewer cases of diabetes and HF, higher ejection fraction, and fewer left anterior descending infarcts). Well-collateralized patients also reached the primary end point less often (18.0% vs 25.4% in the PCI arm; 15.9% vs 18.7% in the MED arm), although this trend did not quite reach statistical significance. On multivariate analyses, however, the presence of collaterals did not independently predict the primary end point or death. When looking at secondary outcomes, there was no impact on reinfarction, although there were fewer deaths and less HF in well-collateralized patients. This association did not remain significant on multivariate analysis.

**Conclusions:** In patients recovering from MI, angiographically visible collaterals were associated with reduced risk of HF and death but not reinfarction. Well-collateralized patients had a lower risk profile, but the presence of collaterals was not an independent predictor of outcomes. Infarct vessel recanalization showed no benefit over MED after accounting for the presence or absence of collaterals.

**Reviewer's Comments:** OAT has been criticized for excluding high-risk patients. The accompanying editorial by Chatterjee stresses that point, noting that medical therapy works well in low- and moderate-risk post-MI patients. He also cites a large meta-analysis suggesting that late PCI of occluded infarct vessels can be associated with improved survival. The present authors note evidence that collaterals are protective during acute MI and are associated with reduced infarct size and higher ejection fraction. In the current analysis of subacute MI patients, visible collaterals were associated with less HF and reduced long-term mortality but no reduction in reinfarction. They suggest rapid regression of collaterals post-PCI and high rates of vessel reocclusion as possible contributing factors. Because collaterals did not independently predict prognosis, the authors attribute their association with better outcomes to confounding by baseline clinical variables, which, they believe, are largely responsible for those outcomes. It seems that the opposite could as easily be true, with collaterals being the true main determinant of outcome. (Reviewer-Gregg S. Pressman, MD).

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Keywords: Visible Collaterals, Post-MI, Prognosis

#### **Gender May Affect Benefit From ICD**

Gender Differences in Clinical Outcome and Primary Prevention Defibrillator Benefit in Patients With Severe Left Ventricular Dysfunction: A Systematic Review and Meta-Analysis.

Santangeli P, Pelargonio G, et al:

Heart Rhythm 2010; 7 (July): 876-882

Women in implantable cardioverter-defibrillator (ICD) trials have more advanced disease than their male counterparts and do not appear to derive the same benefits from ICD implantation for the primary prevention of sudden cardiac death.

**Background:** Women are notoriously under-represented in cardiac clinical trials. It is unclear whether implantable cardioverter-defibrillator (ICD) implantation for the primary prevention of sudden cardiac death (SCD) provides similar benefits for women as for men.

**Objective:** To evaluate the benefit of primary prevention ICD implantation in women.

**Methods:** A meta-analysis was performed on all prospective, randomized trials involving ICD implantation for the primary prevention of SCD in which outcomes for women were reported.

**Results:** Data from the MADIT-II, MUSTT, SCD-HeFT, DEFINITE, and COMPANION trials were included, for a total of 1630 women in the combined study population. Women were more likely to be nonwhite and to have more advanced cardiac disease than men. The mean ejection fraction was 24%, with a mean follow-up of 41 months (both similar to those in men). Women had the same overall mortality as men. Women, however, had a significantly lower incidence of appropriate ICD therapies and did not experience the reduction in mortality with ICD therapy that men appreciated.

**Conclusions:** Women do not appear to benefit as substantially from ICD implantation for the primary prevention of SCD.

**Reviewer's Comments:** This study represents the largest analysis of women and ICD therapy published to date. Any post-hoc analysis limits the conclusions that can be drawn. However, this analysis does draw into question the current practice of gender-blind ICD implantation. It suggests that, while women may die of heart failure with the same frequency as men, the mode of their death appears less often arrhythmic, limiting their benefit from ICD implantation. Of concern is that women in these studies had more advanced, but less ischemic, heart disease and more comorbidities than men. It is possible that studies with more balanced illness severity between genders would show more similar results between genders. Multiple studies have shown that women receive less aggressive cardiac care than men and develop more complications from cardiac procedures. Further study is necessary before changes in practices are made that could prevent women who did receive clinical benefit from receiving appropriate therapy. (Reviewer-Sumeet K. Mainigi, MD).

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Keywords: ICD, Sudden Cardiac Death, Gender



Comparison of Automated Oscillometric Versus Auscultatory Blood Pressure Measurement.

Landgraf J, Wishner SH, Kloner RA:

Am J Cardiol 2010; 106 (August 1): 386-388

There is a statistically significant difference between blood pressure readings measured simultaneously with an automated oscillometric device and a mercury manometer.

**Background:** An accurate blood pressure (BP) measurement is critical in the management of hypertensive patients, and appropriate control of BP decreases adverse cardiovascular events.

**Objective:** To assess the consistency between measuring BP with an automated oscillometric device and a mercury manometer.

**Participants/Methods:** BP was measured in 337 consecutive patients during a routine clinic visit. An appropriate size cuff was attached with a Y-connector to both an automatic oscillometric BP device and a mercury manometer. A senior cardiologist recorded the BP simultaneously by auscultation and with the automated device. Paired *t*-tests were used to determine the statistical significance of the BP differences between the automated oscillometric and the mercury manometer readings.

**Results:** The mean age of patients was  $70.0 \pm 13.4$  years. Significant differences in systolic BP measurements were observed in 22% of all patients. The mean difference between the 2 techniques in measuring the systolic BP was  $1.95 \pm 5$  mm Hg (range, 1 to 26 mm Hg) and was higher with the use of the mercury manometer technique. Differences in diastolic blood pressure measurements were seen in 20% of all patients, with mean values being higher when the mercury manometer technique was used (*P* <0.0001). The mean difference in measuring the diastolic BP with the 2 techniques was  $1.3 \pm 4$  mm Hg (range, 1 to 25). A difference between the 2 measurements was observed in both women and men and tended to be higher in patients with risk factors or established cardiovascular disease. While in patients aged <65 years, 10.4% demonstrated measurement differences between the 2 techniques, in patients aged ≥65 years, significant differences were found in 28.6%.

**Conclusions:** The automated oscillometric device underestimated both the systolic and diastolic BP measurements; this difference tended to be higher in patients aged ≥65 years and in patients with risk factors or established cardiovascular disease.

**Reviewer's Comments:** In this study, Landgraf et al. elegantly proved that there are discrepancies between the systolic and diastolic BP measurements between the electronic and manual techniques. Although the overall mean difference between the 2 measurements was approximately 2 mm Hg, for many patients, the absolute difference was much higher. Underestimating the BP with the use of an electronic device might lead to under-treatment of hypertension, especially in patients aged  $\geq 65$  years and those with risk factors or established cardiovascular disease. (Reviewer-Raul Moldovan, MD).

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Keywords: Blood Pressure, Measurement Techniques

# Eptifibatide Equal to Abciximab During PCI for STEMI

Randomized Comparison of Eptifibatide Versus Abciximab in Primary Percutaneous Coronary Intervention in Patients With Acute ST-Segment Elevation Myocardial Infarction: Results of the EVA-AMI Trial.

Zeymer U, Margenet A, et al:

J Am Coll Cardiol 2010; 56 (August 3): 463-439

In this randomized trial, the small molecule glycoprotein IIb/IIIa inhibitor eptifibatide was found to be noninferior to the "gold standard" abciximab during primary percutaneous coronary intervention for ST-segment elevation myocardial infarction.

**Background:** Glycoprotein (GP) IIb/IIIa receptor blockers are potent intravenous inhibitors of platelet function often administered during percutaneous coronary intervention (PCI). Randomized trials have demonstrated a reduction in peri-procedural ischemic complications with their use. This is perhaps most relevant during primary PCI, when platelets are activated by spontaneous plaque rupture. Abciximab (ReoPro) has proven efficacy in improving reperfusion and short-term ischemic outcomes in the setting of primary PCI for ST-segment elevation myocardial infarction (STEMI). One study also demonstrated a 12-month mortality advantage. The more frequently used, less expensive, and less extensively studied GP IIb/IIIa inhibitor, eptifibatide (Integrilin), has been shown to have similar outcomes in observation studies. It has not been compared to abciximab in a randomized primary PCI study.

**Objective:** The purpose of this noninferiority study was to compare the efficacy of eptifibatide to abciximab in a prospective randomized trial of primary PCI for STEMI.

**Methods:** This multicenter European trial included patients with STEMI who were candidates for primary PCI with adjunctive GP IIb/IIIa inhibitor use (in addition to heparin or enoxaparin, aspirin, and clopidogrel loading dose). Patients presenting within 12 hours of symptom onset without high risk for bleeding and with a glomerular filtration rate >30 mL/min were included. Angiography was performed at least within 2 hours of randomization. The primary end point was reperfusion as indicated by >70% resolution of ST-segment elevation. Secondary end points included additional markers of reperfusion such as infarct-artery patency, TIMI flow grade, and myocardial blush grade, as well as bleeding.

**Results/Conclusions:** Between November 2006 and May 2007, 427 STEMI patients in France and Germany were randomized; of these, 381 patients fulfilled the inclusion criteria. The major finding was no significant difference in the percentage of patients with complete ST-segment resolution (62.6% of the eptifibatide group and 56.3% of the abciximab group), thus meeting the threshold for noninferiority. The only significant difference in clinical outcomes was fewer re-infarctions with eptifibatide (0.4% vs 3.5%; P = 0.03) noted at 30 days and extending to 180 days. There was also a nonsignificant increase in 30-day bleeding complications with eptifibatide (4.0% vs 2.0%; P = 0.27). The authors note that the study was not sufficiently powered to assess these clinical outcomes.

**Reviewer's Comments:** Although eptifibatide has been frequently used in the United States during primary PCI, its efficacy in reperfusion has not been compared to the more extensively studied abciximab in a randomized trial. The primary end point was ST-segment resolution, and this has been associated with perfusion and reduced mortality. However, this study was admittedly underpowered to detect differences in long-term clinical outcomes such as death and reinfarction. This would have required a much larger population. Although these 2 drugs are very different on a molecular and pharmacokinetic level, they seem to provide similar efficacy in terms of reperfusion. (Reviewer-Parul B. Patel, MD).

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Keywords: PCI, ST-Segment Elevation MI

# Exercise Often Worsens PHT in Degenerative MR

Exercise Pulmonary Hypertension in Asymptomatic Degenerative Mitral Regurgitation.

Magne J, Lancellotti P, Piérard LA:

Circulation 2010; 122 (July 6): 33-41

In patients with pulmonary hypertension, pathophysiology at rest is often a poor surrogate for pathophysiology during exercise.

**Background:** Repair of asymptomatic severe mitral regurgitation (MR) remains controversial. Current guidelines recommend surgery for MR with preserved left ventricular (LV) function if pulmonary hypertension (PHT; systolic >50 at rest or >60 with exercise) is present; however, this is based on expert opinion (level of evidence, C).

**Objective:** The current study evaluated the impact of exercise PHT on symptom-free survival in patients with severe, degenerative MR.

Participants/Design: 78 patients were prospectively studied.

**Methods:** All patients had preserved LV systolic function (end-systolic diameter <45 mm and ejection fraction >60%), and moderate MR (effective regurgitant orifice [ERO] area >20 mm2 or regurgitant volume [RV] >30 mL). These patients were referred for bicycle stress echocardiography.

**Results:** Exercise PHT was more frequent than resting PHT (46% vs 15%; P <0.0001). Patients with exercise PHT had higher resting LV end-diastolic volume, resting E/Ea ratio, and exercise E-wave velocity versus those without PHT. Systolic pulmonary arterial pressure (SPAP) increased more in subjects with exercise PHT (30.5 ± 13 mm Hg vs 15 ± 7; P < 0.0001). ERO and RV were similar between groups at rest but were higher during exercise in the exercise PHT group. E/Ea was the only independent predictor of resting SPAP, whereas age, resting SPAP, and exercise ERO were all independent predictors of exercise SPAP and exercise PHT. Subjects with exercise PHT had significantly greater exercise-induced increases in MR than those without (ERO: 12.4 ± 2.2 vs -1.2 ± 1.6 mm2; P < 0.0001; RV: 13.8 ± 3.2 vs -7.6 ± 2.6 mL; P < 0.0001). Over a mean follow-up of 19 ±14 months, 38 patients (49%) developed symptoms. Overall, symptom-free survival was 71% ± 5% and 54% ± 6% at 1 and 2 years, respectively. Clinical variables did not predict symptoms. However, several echocardiography variables did; in particular, exercise-induced changes in ERO ( $12 \pm 13$  vs  $-2 \pm 10$ mm2; P < 0.0001) and RV (13 ± 19 vs -8 ± 17 mL; P < 0.0001) were higher in those who developed symptoms. On multivariate analysis, exercise SPAP and exercise PHT remained independently associated with the development of symptoms. Receiver-operating characteristic curve analysis revealed that exercise PHT was significantly more accurate in predicting the development of symptoms than resting PHT. Exercise SPAP >56 mm Hg was associated with the best specificity (73%), sensitivity (82%), positive predictive value (72%), and negative predictive value (80%).

**Conclusions:** Exercise PHT is frequent in asymptomatic patients with organic MR and is more accurate in predicting the development of symptoms than is resting PHT. Exercise stress echocardiography is very useful in the evaluation of asymptomatic patients with moderate to severe degenerative MR.

**Reviewer's Comments:** This careful work emphasizes the importance of exercise pathophysiology in the development of symptoms among patients with organic MR. All too often we evaluate patients only at rest when making decisions about treating valvular disease. Most patients are active, and symptoms first appear during exercise. While correct performance of exercise Doppler echocardiography takes some skill, it is well worth the effort. (Reviewer-Gregg S. Pressman, MD).

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Keywords: Degenerative Mitral Regurgitation, Exercise, Pulmonary Hypertension

# **Provocative Results Should Stimulate Future Research**

Effect of Hydroxymethylglutaryl Coenzyme-A Reductase Inhibitors on the Long-Term Progression of Rheumatic Mitral Valve Disease.

Antonini-Canterin F, Moura LM, et al:

Circulation 2010; 121 (May 18): 2130-2136

Vascular atherosclerosis and valvular calcification, rheumatic or degenerative, share many similarities.

**Background:** Rheumatic disease is the most common cause of mitral stenosis (MS). Calcification of the valve is a highly organized process involving bone formation pathways and neoangiogenesis. Inflammation underlies these events and C-reactive protein (CRP) levels seem to predict MS progression. Vascular atherosclerosis shares many similarities, and a previous study suggests statins may reduce progression of rheumatic aortic valve disease.

**Objective:** This research looked for associations between statin therapy and MS progression.

**Participants/Methods:** Using a 20-year database, 315 patients with rheumatic MS were identified who had serial echocardiograms and no valvular intervention. Of these, 35 (11.1%) were on statins, while 280 (88.9%) were not. The mean follow-up period was  $6.1 \pm 4.0$  years. Baseline mitral valve area (MVA) and mean gradient were similar between the 2 groups.

**Results:** MVA decreased less in statin-treated patients (0.027 ± 0.056 cm2/year vs 0.067 ± 0.082 cm2/year; *P* =0.005). Rapid progression of MS (>0.08 cm2/year) occurred in 3 statin-treated patients (8.6%) versus 83 untreated patients (29.6%) (*P* =0.008). Similarly, change in mitral gradient was lower in statin-treated patients (0.20 ± 0.59 mm Hg/year vs 0.58 ± 0.96 mm Hg/year; *P* =0.023). Worsening of mitral regurgitation ≥1 grade occurred in fewer statin-treated patients (*P* =0.008). Seventeen percent of patients in the statin group had an increase in systolic pulmonary artery pressure of >10 mm Hg versus 40% in the nonstatin group (*P* =0.045). On single-variable analysis and multivariable regression analysis, statin therapy was a significant predictor of disease progression.

**Conclusions:** In this retrospective study, statin therapy was associated with slower progression of rheumatic mitral valve disease. Given the high prevalence and severe consequences of rheumatic MS in the developing world, statins, as a treatment, offer the prospect of great clinical benefit. Prospective studies need to be done to confirm benefit.

**Reviewer's Comments:** The idea of using statins to delay or halt the progression of valvular disease is not new. However, the prospective trials in calcific (degenerative) aortic stenosis (SALTIRE, SEAS, and RAAVE) have yielded conflicting results. The authors of this study suggest that rheumatic disease, because of more intense underlying inflammation, may better respond to the anti-inflammatory effects of statins. However, we need prospective, randomized data to prove this. The current study was not randomized and did not have progression of disease as a prospectively stated end point. In addition, the number treated with statins was small, and multiple different drugs were used. Nevertheless, the results are provocative and should serve to stimulate future research. (Reviewer-Gregg S. Pressman, MD).

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Keywords: Rheumatic Mitral Stenosis, Statin Therapy, Disease Progression

# Newer Antiplatelet Treatments for ACS Are Reviewed

Advances in Antiplatelet Treatment for Acute Coronary Syndromes. Eshaghian S, Shah PK, Kaul S:

Heart 2010; 96 (May): 656-661

This article examines the role of 3 antiplatelet agents (clopidogrel, prasugrel, and ticagrelor) in the treatment of acute coronary syndrome.

**Clopidogrel:** Clopidogrel is a thienopyridine that irreversibly blocks the adenosine diphosphate (ADP) receptor P2Y12 on the platelets. It is a prodrug that requires hepatic activation. Its effect lasts for the life of the platelet and requires discontinuation at least 5 days before surgery. The CURE trial showed a statistically significant reduction in the primary end point of cardiovascular death, nonfatal MI, or nonfatal stroke with dual antiplatelet therapy, and the major benefit stemmed from a reduction in non-fatal MI. Clopidogrel is approved by the Food and Drug Administration for reduction of atherosclerotic events in patients with non-ST-segment elevation myocardial infarction (non-STEMI), who are medically managed or managed with percutaneous coronary intervention (PCI). The authors recommend its use for medical management of non-STEMI or STEMI acute coronarv syndrome (ACS) and for patients at high risk for bleeding (elderly [>75 years old], low body weight [<60 kg], and a history of prior cerebrovascular accident); they also recommend withholding the drug at least 5 days before elective coronary artery bypass grafting (CABG) or other surgery. Prasugrel: Prasugrel is an irreversible blocker of the ADP receptor P2Y12 on the platelets. It has a more rapid onset of action and a stronger inhibitory effect than clopidogrel. It is a prodrug and requires hepatic activation. The TRITON-TIMI 38 showed a statistically significant reduction in the primary outcome (composite of cardiovascular death, nonfatal MI, or nonfatal CVA) in the prasugrel group over clopidogrel. However, the loading dose used in the trial was lower than the dose commonly used in clinical practice. Patients >75 years of age, with a body weight of <60 kg and a history of prior CVA/transient ischemic attack (TIA) had a higher risk of non-CABG-related TIMI major bleeding compared with the overall trial cohort, thus the "boxed warning" on prasugrel to avoid its use in this high-risk population. The authors recommend its use for patients with STEMI undergoing PCI, recurrent ischemic events on clopidogrel, and stent thrombosis on clopidogrel. They also recommend withholding its use at least 7 days before elective CABG or other surgery. Ticagrelor: Ticagrelor is an orally active drug that reversibly binds the P2Y12 receptor. It is not a thienopyridine, and it is not a prodrug. Ticagrelor has a shorter half-life of approximately 12 hours and requires twice daily dosing. The PLATO Trial showed a statistically significant reduction in the primary end point of vascular death, nonfatal MI, or nonfatal stroke: no statistically significant bleeding was observed in the overall population. The authors recommend its use in the medical/invasive management of STEMI or non-ST-elevation ACS, bridging therapy for patients on clopidogrel/prasugrel before elective surgery, and cautious use in patients with chronic obstructive pulmonary disease/acute dyspnea, hyperuricemia, and bradyarrhythmias; it should be withheld 3 days before elective CABG or other surgery.

**Reviewer's Comments:** Nice review article examining the role of 3 antiplatelet agents (clopidogrel, prasugrel, and ticagrelor) in ACS using data from the original trials (ie, CURE [clopidogrel], TRITON-TIMI 38 [prasugrel], and PLATO [ticagrelor]). Good boxed summary recommendations are at the end. (Reviewer-Sahil Mehta, MD).

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Keywords: ACS, Antiplatelet Agents

# **Enhanced External Counterpulsation Improves Angina Class**

Impact of Enhanced External Counterpulsation on Canadian Cardiovascular Society Angina Class in Patients With Chronic Stable Angina: A Meta-Analysis.

Shah SA, Shapiro RJ, et al:

Pharmacotherapy 2010; 30 (July): 639-645

Enhanced external counterpulsation improves the Canadian Cardiovascular Society angina class in 86% of patients with chronic stable angina.

**Background:** The primary treatment for angina pectoris is medical therapy with or without percutaneous coronary intervention (PCI) and/or coronary artery bypass graft (CABG) surgery. One year after revascularization, nearly 30% of patients continue to experience angina. Enhanced external counterpulsation (EECP) is a noninvasive therapy that alleviates angina, enriches quality of life, and extends time to exercise-induced ischemia. The Canadian Cardiovascular Society (CCS) angina class, a marker of disease progression in coronary artery disease patients, groups individuals based on functional limitations associated with level of exertion. It is a frequent outcome measure in EECP studies.

**Objective:** To ascertain the effect of EECP on CCS angina class in patients with chronic stable angina. **Design:** Meta-analysis.

Participants: 949 patients with chronic stable angina who underwent EECP were included.

**Methods:** The researchers performed a search (1950 to February 7, 2009) of English language studies in MEDLINE, EMBASE, and Cumulative Index to Nursing and Allied Health Literature databases using EECP, enhanced external counterpulsation, and counterpulsation as the medical subject heading terms and key words. The CCS classes reported before and immediately after (within 1 month) 35 1-hour EECP sessions were compared. To eliminate potential data duplication, numerous studies by EECP data registries (the International EECP Patient Registry and the EECP Consortium) were excluded.

**Results:** 13 studies of 949 patients with CCS angina class data were included in this meta-analysis. CCS angina class improved by at least 1 class in 86% of patients (95% CI, 82% to 90%; P = 0.008). This benefit was maintained after omitting the 2 largest studies and when using a fixed-effects model. The degree of benefit with baseline CCS classes 3 to 4, 2 to 4, and 1 to 4 was 90% (95% CI, 73% to 99%), 83% (95% CI, 75% to 90%), and 87% (95% CI, 84% to 90%), respectively. Among studies in which at least 60% of patients had a prior PCI and CABG, 88% of patients had an improvement of at least 1 CCS class (95% CI, 0.74 to 0.97). The Egger bias statistic revealed no publication bias (P = 0.97).

**Conclusions:** 86% of chronic stable angina patients treated with EECP achieve improvement in CCS class angina.

**Reviewer's Comments:** More than 9.8 million Americans have angina pectoris. Despite best medical practices with drug management, PCI, and/or CABG, a significant number of these individuals will continue to suffer with symptoms. The results of this meta-analysis indicated that 86% of patients undergoing EECP respond favorably. The magnitude of benefit from this analysis is limited to immediately after completion of EECP. In other published studies, comparable benefits were maintained in 74% of patients at 3 years, and 81% of initial responders remained free of major adverse cardiac events and the need for revascularization at 5 years. Additional long-term studies are warranted to clarify the position of EECP in the treatment strategies to manage chronic stable angina. (Reviewer-Debra L. Braverman, MD).

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Keywords: Enhanced External Counterpulsation, Angina Pectoris

#### **BBB** Associated With Poor Prognosis

Prognostic Implications of Bundle Branch Block in Patients Undergoing Primary Coronary Angioplasty in the Stent Era. Vivas D, Pérez-Vizcayno MJ, et al:

Am J Cardiol 2010; 105 (May 1): 1276-1283

Bundle branch block is a poor prognostic factor in ST-segment elevation myocardial infarction.

**Background:** In the past, bundle branch block (BBB) in patients with ST-segment elevation myocardial infarction (STEMI) has been associated with a poor prognosis. In the current era of rapid angioplasty and stenting in the setting of acute STEMI, no clear data exist on the prognostic value of BBB.

**Objective:** To assess the prognostic value of BBB with angioplasty-treated STEMI. Also, the prognostic value regarding the type of BBB (right, left, previously documented, persistent or transient) was evaluated. **Design:** Observational, single-center study.

**Methods:** Data for 913 consecutive patients presenting with STEMI and treated with primary percutaneous coronary intervention (PCI) were analyzed. Patients with a paced rhythm or who required rescue percutaneous coronary intervention (PCI) status post-failed thrombolysis were excluded. Clinical, electrocardiographic, and angiographic data were prospectively obtained. The primary end point (short- and long-term) was defined as a combined outcome of death and reinfarction, with a median follow-up period of 19 months.

**Results:** 140 of the 913 patients (15%) had BBB. Right BBB (RBBB) was seen in 119 patients (13%), of which 27 (23%) were previous, 45 (38%) were persistent, and 47 (39%) were transient. Left BBB (LBBB) was seen in 21 patients (2%), of which 8 (38%) were previous, 9 (43%) were persistent, and 4 (19%) were transient. Patients with BBB were significantly older, had more frequent anterior infarctions, diabetes, a greater Killip class, and a lower left ventricular ejection fraction (P < 0.005 for all). They also had greater mortality compared to patients without BBB (P < 0.005). The primary outcome occurred more frequently in patients with persistent RBBB/LBBB compared to those with previous or transient RBBB/LBBB. Multivariate analysis revealed that persistent RBBB/LBBB was an independent predictor of death and reinfarction.

**Conclusions:** In patients undergoing PCI status post-STEMI, BBB is associated with both a poor short- and long-term prognosis. This poor prognosis is mainly high among patients with persistent BBB.

**Reviewer's Comments:** BBB in the setting of STEMI was associated with a poor prognosis in the prethrombolytic and thrombolytic era. However, this paper illustrates that this unfavorable prognosis is also present in the setting of primary angioplasty and stenting. It is interesting that only persistent BBB, and not previous or transient BBB, is associated with increased combined short- or long-term mortality and reinfarction. The mechanism for this is unclear. Both branches are supplied from coronary vessels arising from proximal coronary arteries, and BBB may, therefore, be indicative of larger infarctions. Also, the right bundle branch has a dual blood supply, meaning a RBBB would theoretically involve disease of 2 main coronary arteries. Of note, patients with a persistent BBB also had greater peak enzymes and a greater incidence of stent thrombosis, malignant arrhythmia, and major bleeding. (Reviewer-Suraj Maraj, MD).

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Keywords: Bundle Branch Block, Prognosis, ST-Segment Elevation Myocardial Infarction

# Significant Association Between Statin Use and Decreased Incidence of AF

Association Between Statin Use and the Incidence of Atrial Fibrillation Following Hospitalization for Coronary Artery

Disease.

Kulik A, Singh JP, et al:

Am J Cardiol 2010; 105 (June 15): 1655-1660

Statin use may be beneficial as an antiarrhythmic in decreasing the incidence of atrial fibrillation after myocardial infarction or coronary revascularization.

**Background:** Atrial fibrillation (AF) is a common and increasingly prevalent condition that may be triggered by inflammation with subsequent structural remodeling. Current data suggest that statins may possess antiarrhythmic properties that may prevent AF.

**Objective:** To assess the association between statin use and new-onset AF in a large cohort of patients after hospitalization for treatment of coronary artery disease (CAD).

**Methods:** Data on Medicare beneficiaries (≥65 years of age) who had hospitalizations for acute myocardial infarction (MI) or coronary revascularization between January 1, 1995, and December 31, 2004, were reviewed. Only patients who participated in 1 of 2 government-sponsored medication benefit programs were included. Any patients with a history of AF before and during hospitalization were excluded.

**Results:** The study cohort included 29,088 patients. New-onset AF was compared between patients who were (n=8,450) and were not (n=20,638) prescribed statins within 30 days of hospital discharge after their cardiac event. In patients who received statins, the rates of new-onset AF at 5 and 10 years were 32.6% and 51.2%, respectively. New-onset AF for the same time periods was 38.3% and 58.0%, respectively, in patients who did not receive statins. After controlling for demographic and clinical confounders, multivariable analysis revealed that statin use independently decreased the risk of developing new-onset AF compared to nonusers (adjusted HR, 0.90; 95% CI, 0.85 to 0.94). After adjustment for propensity-score and health-seeking behaviors, similar results were obtained.

**Conclusions:** Following MI or coronary revascularization, initiating statin therapy within 30 days after hospital discharge is independently associated with a decrease in the risk of new-onset AF.

**Reviewer's Comments:** The beneficial effects of statin usage in patients with cardiovascular disease is well documented. Statins decrease cardiovascular events and increase survival. However, the use of statins to prevent AF in patients with CAD has not been well elucidated. The pathogenesis of AF is multifactorial, but inflammation may be a triggering event, with subsequent electrophysiological and structural remodeling creating the ideal substrate for AF. Since statins may have both anti-inflammatory and antisympathetic properties, they may, therefore, be beneficial in decreasing the incidence of AF. This study is the largest to-date that assesses the impact of statins for the primary prevention of AF. The study cohort importantly includes elderly patients with active CAD and who are predominantly women. There was a significant association between statin use and a decrease in the incidence of AF. Since current practice guidelines already recommend statin use in patients with active cardiovascular disease, this study should not alter practice guidelines. However, while the study does not imply a cause-and effect relationship, it is tantalizing evidence of yet another beneficial effect of statins, possibly via cell membrane ion channel stabilization. (Reviewer-Suraj Maraj, MD).

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Keywords: Statins, Antiarrhythmic, Coronary Artery Disease, Atrial Fibrillation

# PCI Timing Is of the Essence

Impact of Delay to Angioplasty in Patients With Acute Coronary Syndromes Undergoing Invasive Management: Analysis From the ACUITY (Acute Catheterization and Urgent Intervention Triage strategY) Trial.

Sorajja P, Gersh BJ, et al:

J Am Coll Cardiol 2010; 55 (April 6): 1416-1424

A delay from presentation of >24 hours is associated with adverse outcomes in patients with non–ST-segment elevation acute coronary syndromes.

**Background:** Although there is general consensus that an early invasive strategy provides better outcomes in moderate- to high-risk patients with non–ST-segment elevation acute coronary syndromes (NSTE-ACS), the optimal timing of angiography and revascularization is not known.

**Objective:** To evaluate the best timing of revascularization utilizing percutaneous coronary intervention (PCI) after clinical presentation in patients with NSTE-ACS.

Methods: The Acute Catheterization and Urgent Intervention Triage strategY (ACUITY) trial was a large, randomized trial that investigated 3 antithrombotic regimens: (1) unfractionated or low molecular weight heparin plus a glycoprotein IIb/IIIa inhibitor; (2) bivalirudin plus a glycoprotein IIb/IIIa inhibitor; or (3) bivalirudin alone. This investigation examined the effect of timing of percutaneous coronary intervention (PCI) on outcomes in 7749 ACUITY patients that had a known angiography time. Patients were separated into 3 approximately equally sized groups based on time from presentation to revascularization with PCI: <8 hours, 8 to 24 hours, and ≥24 hours.

**Results:** Those with PCI >24 hours from presentation had higher rates of death and MI at 30 days when compared to those with earlier PCI. The increase in mortality and combined death or MI for this group persisted at 1 year. A delay >24 hours was a strong independent predictor of adverse outcomes after multivariable adjustment for baseline differences. Patients with intermediate (3 to 4) and high (5 to 7) Thrombolysis in Myocardial Infarction (TIMI) risk scores and a delay of >24 hours had significant increases in 30-day death and death or MI. One-year mortality was increased in those with a delay of >24 hours regardless of baseline TIMI score; the greatest difference was evident in the higher risk patients. The rate of non-coronary artery bypass grafting major bleeding was lower with bivalirudin alone compared with a glycoprotein IIb/IIIa inhibitor-based regimen, regardless of time to PCI.

**Conclusions:** According to the authors, "...delaying revascularization with PCI >24 hours in patients with NSTE-ACS was an independent predictor of early and late mortality and adverse ischemic outcomes." **Reviewer's Comments:** This investigation shows a strong independent association of PCI delay of >24 hours from presentation of NSTE-ACS with increased mortality and adverse outcomes. The risk was most pronounced in high-risk patients, but even low-risk patients (TIMI score, 0 to 2) had increased mortality at 1 year with >24 hour delay from presentation to PCI. There were differences in baseline characteristics between the groups; those that underwent PCI >24 hours after presentation more frequently had elevated troponins, high TIMI scores, left main culprit, prior CABG, and baseline TIMI flow grade 3 (among other differences). Although multivariable adjustment was used to correct for measured differences, the authors acknowledge that unmeasured confounders cannot be excluded. As is suggested, it is not known whether a delay to angiography reflects a more stable patient or one too ill to undergo earlier angiography. Despite the limitations of a post-hoc study, the findings are suggestive and large scale randomized trials are needed to help definitively answer the question of timing of angiography and PCI in NSTE-ACS patients. (Reviewer-Stephen Olex, MD).

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Keywords: Acute Coronary Syndrome, Invasive Management, Angioplasty

# WCDs Offer Temporary Option in Patients at Risk for SCD

Aggregate National Experience With the Wearable Cardioverter-Defibrillator: Event Rates, Compliance, and Survival. Chung MK, Szymkiewicz SJ, et al:

J Am Coll Cardiol 2010; 56 (July 13): 194-203

The use of wearable cardioverter-defibrillators is a viable option in certain patient populations.

**Background:** The use of implantable cardioverter-defibrillators (ICDs) has increased over recent decades with the multiple indications for primary and secondary prevention of sudden cardiac death (SCD). There are situations, however, that necessitate the deferment of ICD implantation either due to guidelines (ie, waiting 40 days after an acute myocardial infarction [MI]), or other issues, such as transient infection. Many patients are at risk of SCD during the waiting period. The use of wearable cardioverter-defibrillators (WCDs) has increased in these populations but without the backing of evidence-based data.

**Objective:** To assess the efficacy of WCDs in the prevention of SCD due to ventricular tachycardia or ventricular fibrillation (VT/VF).

**Methods:** An analysis of data collected by a WCD manufacturer (ZoII) of all patients who used ZoII WCD in the United States over a 4-year period was conducted. Demographic data, as well as daily use information and recorded/treated events with outcomes, were analyzed. Efficacy in the prevention of SCD was compared to that of patients undergoing first ICD implantation. Rhythm strips of each recorded clinical event were analyzed for appropriateness of device action/inaction.

**Results:** 3569 patients, who wore a WCD for at least 1 day, were included in the analysis. Baseline demographics available for 2731 of the patients revealed a mean age of 59 years (range, 12 to 93 years). The indication for use was unavailable in 838 patients. The most common indication (23%) was in patients with explanted ICDs awaiting reimplantation. Total use was 143,643 patient-days (mean, 53 days; range, 1 to 1590 days). The mean daily use was 20 hours. Compliance with daily use was 90% in 52% of the patients and 80% in 71% of the patients. There were 307 patients (14%) who stopped wearing the WCD prematurely, mostly due to device discomfort. A longer duration of use correlated with better compliance. A total of 80 sustained VT/VF episodes were recorded in 59 individuals (1.7%) while wearing the WCD (49 episodes occurred in ICD-explant patients). The success of the first device shock in terminating the arrhythmia was 76/76 (100%) in unconscious patients and 99% for all patients. Eight patients eventually died despite successful defibrillation and restoration of consciousness mostly due to recurrent VT/VF (89.5% survival). The device also recorded 26 episodes of asystole or other non-VT/VF rhythms resulting in 20 deaths. Inappropriate shocks occurred in 67 patients (2%). The overall acute-survival rate was 99% (90% for those with ventricular tachy-arrhythmias). Comparison of survival outcomes in WCD versus a control group of ICD patients showed similar 3-year and 3-month survival rates.

**Conclusions:** WCD use was tolerated by most patients and mortality data were favorable when compared with ICD patients.

**Reviewer's Comments:** WCDs appear to provide a reasonable temporary option for patients at risk for SCD but who are not able to get ICDs. (Reviewer-Khalid Almuti, MD).

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Keywords: Wearable Cardioverter-Defibrillators, Sudden Cardiac Death

# **Cocaine-Associated Chest Pain and Beta-Blockers -- Urban Legend?**

β-Blockers for Chest Pain Associated With Recent Cocaine Use.

Rangel C, Shu RG, et al:

Arch Intern Med 2010; 170 (May 24): 874-879

In the emergency department,  $\beta$ -blocker use in cocaine-associated chest pain may be safe.

**Background:** Cocaine inhibits reuptake of catecholamines and also acts as a sodium channel blocker. Due to these properties, cocaine can cause myocardial ischemia, infarction, life-threatening arrhythmia, and severe hypertension. Even though  $\beta$ -blockers are very effective in treating these conditions, recent guidelines recommend against using them in cocaine-associated chest pain due to fear of unopposed  $\alpha$ -receptor activation. This assumption is based on case reports and small hemodynamic studies.

**Objective:** To report the short- and long-term outcomes in a group of patients with chest pain and urine toxicology positive for cocaine, who did and did not receive  $\beta$ -blockers.

**Methods:** A retrospective study was conducted of patients presenting to San Francisco General Hospital with chest pain and urine toxicology positive for cocaine.

**Results:** 331 patients were included in the study. Cocaine was used a median of 24 hours before the hospital emergency department (ED) visit. A total of 151 patients (46%) received a  $\beta$ -blocker in the ED; 130 patients (85%) of them received oral or intravenous metoprolol, and 21 patients (14%) received oral or intravenous labetalol. Sixty-five percent of the patients received some type of  $\beta$ -blocker during the hospital stay. There were no significant differences in electrocardiographic changes, troponin levels, length of stay, use of vasopressor agents, intubation, ventricular tachycardia or ventricular fibrillation, or death among those who did and did not receive a  $\beta$ -blocker. After adjusting for potential confounders, systolic blood pressure significantly decreased a mean of 8.6 mm Hg (95% CI, 14.7 to 2.5 mm Hg) in those receiving a  $\beta$ -blockers in the ED compared to patients who received their first  $\beta$ -blocker in the hospital ward. In regard to long-term follow-up (median, 972 days) after adjusting for potential confounders, patients discharged on  $\beta$ -blockers exhibited a significant reduction in cardiovascular death (HR, 0.29; 95% CI, 0.09 to 0.98).

**Conclusions:** The use of  $\beta$ -blockers in cocaine-associated chest pain was not associated with harmful effects and may very well be beneficial.

**Reviewer's Comments:** Cocaine-associated chest pain is a common presentation in the ED, and many of these patients have definite indications for treatment with  $\beta$ -blockers. In general,  $\beta$ -blockers are avoided in this circumstance due to fear of unopposed  $\alpha$ -receptor activation. The above study suggests that these fears are probably unfounded. This is a retrospective study and a randomized controlled trial to confirm this is needed. (Reviewer-Pradeep S. Arumugham, MD).

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Keywords: Cocaine, Chest Pain, β-Blockers

# PCI Associated With Survival in OHCA

Immediate Percutaneous Coronary Intervention Is Associated With Better Survival After Out-of-Hospital Cardiac Arrest: Insights From the PROCAT (Parisian Region Out of Hospital Cardiac Arrest) Registry.

Dumas F, Cariou A, et al:

Circ Cardiovasc Interv 2010; 3 (June): 200-207

Immediate coronary angiography and revascularization is the strongest independent predictor of survival among cardiac arrest survivors without an obvious extracardiac cause.

**Background:** Out-of-hospital cardiac arrest (OHCA) is often caused by acute coronary syndrome (ACS), and, thus, current practice guidelines recommend consideration of coronary angiography with percutaneous coronary intervention (PCI) if ACS is suspected. Given the absence of clinical data, such as symptoms or history, the post-resuscitation electrocardiogram (ECG) is often relied upon to determine whether a patient might benefit from immediate cardiac catheterization. However, the predictive value of the post-resuscitation ECG is poor, and it is possible that a significant proportion of patients who might actually benefit from immediate catheterization would be missed. The Parisian Region Out-of-Hospital Cardiac Arrest (PROCAT) registry has prospectively collected data from a tertiary care center specialized in OHCA management. Unless there is an obvious extracardiac cause of arrest, all stabilized patients presenting to or transferred to this center undergo routine immediate coronary angiography and PCI if a culprit lesion is found.

**Objective:** To assess the impact of immediate angiography followed by revascularization on the survival of patients presenting with OHCA presumed to be due to a cardiac cause.

**Methods:** The PROCAT registry data were collected from 2003 to December 2008 and included all OHCA patients in the Paris region (daytime population, approximately 5 million) treated by local emergency medical services, and in whom, return of spontaneous circulation (ROSC) was achieved. The study population included the patients who subsequently underwent cardiac catheterization and PCI if indicated, followed by specialized post-resuscitation care, including therapeutic hypothermia. The primary outcome was survival at discharge. **Results:** Of the 714 patients with OHCA in whom ROSC was achieved and who were admitted to the tertiary care center, 435 (61%) had no obvious extracardiac cause and comprised the study population. The post-ROSC ECG demonstrated ST-segment elevation in 31%. Of these, 90% of the patients underwent successful PCI. In patients with other ECG patterns, 58% had a significant stenosis, and 85% of these underwent successful PCI. The positive predictive value of the post-ROSC ECG for coronary lesion was 96%, and the negative predictive value was 46%. Overall, hospital survival was 39%. Of these, 94% had little or no neurologic sequelae. The strongest independent predictor of survival was successful PCI. Negative predictors were delay in CPR and delay in ROSC, older age (>59 years), and initial rhythm asystole or pulseless electrical activity.

**Conclusions:** This study demonstrates the association of ACS and OHCA and the benefit effect of immediate revascularization on survival.

**Reviewer's Comments:** The survival of patients who underwent successful PCI was 51%. Although this was a select population within a specialized health-care system, the authors support immediate revascularization in patients with ROSC regardless of ECG findings if a cardiac cause is suspected. This treatment had the greatest impact on survival, although post-resuscitation management, including therapeutic hypothermia, is probably also critical to good outcomes. (Reviewer-Parul B. Patel, MD).

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Keywords: Cardiac Arrest, Percutaneous Coronary Intervention

# Vital Exhaustion May Be Associated With Cardiac Events

Vital Exhaustion As a Risk Factor for Adverse Cardiac Events (From the Atherosclerosis Risk In Communities [ARIC] Study).

Williams JE, Mosley TH Jr, et al:

Am J Cardiol 2010; 105 (June 15): 1661-1665

Symptoms associated with vital exhaustion may be a precursor to a myocardial infarction, especially in women.

**Background:** Vital exhaustion describes a state of excessive fatigue, increased irritability, and demoralization. Support for a positive association with coronary heart disease (CHD) is seen in the European literature. Using data from the Atherosclerosis Risk In Communities (ARIC) study cohort, this analysis compared high and low vital exhaustion patients and their risk of myocardial infarction (MI) and CHD in patients in the United States. **Objective:** To determine if participants with high vital exhaustion compared to their low exhaustion peers are at an increased risk for adverse cardiac events and to look for a monotonic increase in risk from low to high exhaustion with adjustment for known predictors of cardiovascular disease progression.

**Participants/Methods:** Participants were black and white middle-aged men and women (age range, 48 to 67 years). ARIC is a large, population-based, prospective study of the cause and natural history of

atherosclerosis. Baseline examinations were done from 1987 to 1989. Three years later, participants returned for follow up. Hospitalizations and deaths during that time were identified via telephone interviews and hospital surveillance. Participants for this analysis were the 14,348 people who returned for visit 2 from 1990 to 1992. After several exclusions, such as for incomplete data, the final sample was 12,895 patients. Vital exhaustion was assessed using a 21-item questionnaire. Covariates in the regression analysis were age, race, cigarette smoking, level of education, gender, body mass index (BMI), blood pressure, plasma LDL and HDL, and diabetes mellitus.

**Results:** Participants in the highest quartile of vital exhaustion were slightly older, heavier, and more likely to be women and black, with a less than high school education. They also smoked more cigarettes, were more likely to be diabetic and hypertensive, and had higher HDL levels. The highest quartile of vital exhaustion predicted adverse cardiac events in age-, gender-, and race-adjusted analyses. After adjustment for education level, monotonically from the lowest to the highest quartile, BMI, LDL, HDL, blood pressure, smoking, and diabetes, the hazard ratio was attenuated but remained statistically significant. Risk for adverse cardiac events increased.

**Conclusions:** Vital exhaustion is associated with several metabolic, hemodynamic, and immune responses important in the development and progression of CHD. Exhaustion is a common precursor to MI in women. There is an inverse relationship between exhaustion and socioeconomic status. People of lower socioeconomic status report more chronic stress. Vital exhaustion is closely linked to depression and may be difficult to separate.

**Reviewer's Comments:** Evaluating patients for vital exhaustion can lead to better care by anticipating which patients are most vulnerable for cardiac events. High vital exhaustion was seen particularly in women and black participants, which can help identify who is at the highest risk. (Reviewer-Marjorie Stanek, MD).

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Keywords: Vital Exhaustion, Risk Factors, Cardiac Events