Not only might sleep apnea cause heart failure, heart failure might cause sleep apnea; in any case sleep apnea is highly prevalent in heart failure.

**Background:** Obstructive sleep apnea (OSA) occurs with periodic upper airway obstruction while central sleep apnea (CSA) involves intermittent failure of respiratory drive due to exaggerated swings in PCO$_2$; both can occur together in patients with heart failure (HF), and the predominant type can shift within an individual.

**Objective:** To test the theory that overnight fluid displacement from the legs to the neck/thorax, in response to recumbency, contributes to both OSA and CSA.

**Methods:** 57 men with stable HF, NYHA class I to III, and ejection fraction (EF) ≤45 were studied. Leg fluid volume (LFV) was measured by bioelectric impedance; right calf and neck circumference were measured (with lines drawn to ensure consistency) before and after sleep. Patients with predominant OSA (≥ 50% obstructive events) and apnea-hypopnea index (AHI) ≥15 were offered continuous positive airway pressure (CPAP).

**Results:** In the OSA-predominant group, there was an inverse relationship between changes in LFV and neck circumference ($r = -0.780; P<0.001$). For the CSA-predominant group, there was also an inverse relationship between changes in LFV and neck circumference ($r = -0.568; P=0.006$), while there was a direct correlation with mean sleep PCO$_2$. Multivariate analysis indicated that LFV was the only significant independent correlate of AHI in both groups. Leg edema was higher and mean sleep PCO$_2$ was lower in the CSA group. Both groups had similar increases in neck circumference and similar frequency of nocturia. However, LFV reduction was twice as great in the CSA group versus the OSA group. Twenty OSA patients received CPAP with significant reductions in AHI and neck circumference ($P<0.001$) but no effect on overnight change in LFV.

**Conclusions:** Overnight change in LFV correlated with AHI in both OSA and CSA, with similar changes in neck circumference in both. LFV correlated inversely with mean sleep PCO$_2$ in CSA only. Fluid shifts from the legs to the neck can contribute to OSA; CPAP prevents the associated increase in neck circumference. In CSA, where CPAP is ineffective, fluid shifts are greater, with an associated fall in mean sleep PCO$_2$, possibly due to increased fluid in the lungs stimulating hyperventilation.

**Reviewer’s Comments:** This research looks at sleep apnea from a novel perspective and invokes night-time fluid shifts in the pathophysiology of both OSA and CSA. The authors note that LFV shift correlated with the amount of edema and sitting time and inversely with activity level, suggesting that exercise might be useful. Perhaps altered timing of diuretics and general measures to improve cardiac and renal function would also help. This is a small study involving only men with heart failure. In addition, unblinded measurements of calf and neck circumference introduce the possibility of bias. Nevertheless, it suggests interesting new ways of understanding the complex pathophysiology of sleep apnea syndromes. (Reviewer-Gregg S. Pressman, MD).

**Keywords:** Heart Failure, Nocturnal Fluid Shifts, Sleep Apnea

**Print Tag:** Refer to original journal article
Serum Biomarkers as Predictors of ST-Segment Recovery Following PCI

Comparison of the Usefulness of N-Terminal Pro-Brain Natriuretic Peptide to Other Serum Biomarkers as an Early Predictor of ST-Segment Recovery After Primary Percutaneous Coronary Intervention.

Verouden NJ, Haeck JD, et al:

Am J Cardiol 2010; 105 (April 15): 1047-1052

NT-pro-BNP levels predict ST-segment recovery following primary percutaneous coronary intervention.

**Background:** Serum biomarkers have prognostic value in patients with acute coronary syndrome. However, there are limited data on their ability to predict microvascular obstruction by ST-segment recovery following primary percutaneous coronary intervention (PCI).

**Objective:** To assess the association between 5 serum biomarkers, obtained before emergency PCI and immediate ST-segment recovery status following primary PCI for ST-segment elevation MI.

**Methods:** N-terminal pro-brain natriuretic peptide (NT-pro-BNP), cardiac troponin T, creatinine kinase-MB fraction, high-sensitivity C-reactive protein, and serum creatinine were obtained through the arterial sheath at the start of primary PCI. Serial 12-lead electrocardiograms were obtained before arterial puncture and at the end of the PCI. The primary outcome analyzed was the presence of incomplete ST-segment recovery (defined as ST-segment recovery of <50%).

**Results:** There were 662 patients with ST-segment elevation MI, and 338 (51%) had incomplete ST-segment recovery. NT-pro-BNP levels that were elevated (≥608 ng/L) were the strongest predictors of incomplete ST-segment recovery (adjusted OR, 2.6; 95% CI, 1.7 to 4.1; \( P < 0.001 \)) when compared to other serum biomarkers and clinical predictors. Also, elevated NT-pro-BNP levels were more strongly predictive in patients with no prior history of coronary artery disease or hypertension (adjusted OR, 4.7; 95% CI, 2.4 to 9.2; \( P < 0.001 \)). NT-pro-BNP was the best contributor when added to a multivariate model with clinical predictors of incomplete ST-segment recovery.

**Conclusions:** Among 5 serum biomarkers, NT-pro-BNP was the strongest independent predictor of ST-segment recovery at the end of primary PCI for ST-segment elevation MI.

**Reviewer's Comments:** This study illustrates that NT-pro-BNP measured before emergent coronary angiography was the strongest, independent predictor of ST-segment recovery when compared to other biomarkers of myocardial cell damage, renal function, and inflammation. Incomplete ST-segment resolution status post-PCI indicates impaired myocardial reperfusion at the microvasculature level. The association between BNP levels pre-PCI and incomplete ST-segment resolution post-PCI is therefore likely indicative of significant left ventricular wall stretch at the beginning of the procedure and persistent abnormalities in microvascular reperfusion at the end of the procedure. Also, subgroup analysis illustrated that this association was even stronger in patients with no prior history of hypertension or coronary artery disease, indicating that the incomplete ST-segment recovery is associated with left ventricular wall stretch from acute ischemia. This study has important clinical implications. A "point-of-care" BNP pre-PCI may help to risk stratify patients and help identify those who may need adjunctive therapy when undergoing PCI. This may include adding a glycoprotein IIb/IIIa inhibitor, post-ischemic conditioning, or circulatory support. A decreased creatinine clearance was also predictive of incomplete ST-segment recovery, but was not as strongly predictive as NT-pro-BNP. (Reviewer-Suraj Maraj, MD).

Keywords: Serum Biomarkers, NT-pro-BNP, ST-Segment Recovery, Coronary Intervention

Print Tag: Refer to original journal article
EECP Improves Blood Pressure

Effects on Blood Pressure in Patients With Refractory Angina Pectoris After Enhanced External Counterpulsation.

Bondesson S, Pettersson T, et al:

Blood Press 2010; April 29 (): epub ahead of print

Refractory angina patients demonstrate improved blood pressure initially after a course of EECP, but these benefits do not persist over the long term.

Background: Enhanced external counterpulsation (EECP) is a noninvasive treatment that reduces angina pectoris symptoms in coronary artery disease. Diastolic augmentation, increase in venous return, and afterload reduction are the immediate hemodynamic effects of EECP. Proposed mechanisms for the long-term benefits of this treatment include improved endothelial function and increased collateral flow. Little is known about the specific effects of EECP on blood pressure.

Objective: To evaluate the arterial blood pressure response to EECP in refractory angina patients immediately after completing a course of treatment and at 12 months follow-up.

Design: Observational cohort study.

Participants: 153 patients with refractory angina pectoris referred for EECP were included; 100 underwent EECP (77 men, 23 women; age range, 47 to 91 years). Fifty-three (41 males and 12 females; age range, 52 to 87 years) did not have EECP for a variety of clinical and logistical reasons and served as a reference group. All were maintained on antianginal pharmacologic therapy including a long-acting nitrate, a β-adrenoceptor antagonist, and/or a calcium antagonist.

Methods: The EECP group underwent 35 ± 2 hours of EECP over 35 days. Systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) were measured at baseline, after the last EECP session, and at the 12-month follow-up. Assessment of treatment effect was blood pressure as measured by SBP, DBP, and mean arterial pressure (MAP). When at least 2 of the 3 parameters (SBP, DBP, and/or MAP) were changed, the patient was defined as having an overall change in blood pressure.

Results: EECP patients had a drop in blood pressure while reference patients had an elevation in blood pressure. MAP, SBP, and DBP were all significantly decreased after EECP (MAP, 94 ± 12 vs 88 ± 11 mm Hg; SBP, 131 ± 21 vs 121 ± 16 mm Hg; DBP, 74 ± 10 vs 69 ± 10 mm Hg; all P < 0.001). There was a correlation between a decrease in blood pressure after EECP and a higher baseline MAP, SBP, and DBP. The changes in blood pressure were not persistent at the 12-month follow-up. Heart rate remained unchanged, and there were no adverse events.

Conclusions: EECP initially improves blood pressure in patients with refractory angina, but this benefit does not persist at 1-year follow-up.

Reviewer's Comments: This is the first study to compare the effect of EECP on blood pressure and heart rate in refractory angina patients with a reference group on optimal antianginal medications. The results show that EECP decreases all blood pressure parameters compared with patients on pharmacologic therapy alone. A decrease in sympathetic tone while lying supine during EECP does not explain this drop in blood pressure as there was no corresponding drop in heart rate. The improvement in blood pressure as a result of EECP may be due to documented improvements in exercise capacity, vasoreactivity, and endothelial function. (Reviewer-Debra L. Braverman, MD).

Keywords: Enhanced External Counterpulsation, Refractory Angina, Blood Pressure

Print Tag: Refer to original journal article
Pericardial fat volume is higher in asymptomatic patients experiencing adverse cardiac events.

**Background:** Pericardial fat has been linked to markers of inflammation, coronary artery risk factors, and severity of coronary artery disease.

**Objective:** To assess the ability of pericardial fat to predict future cardiovascular adverse events.

**Design/Participants:** This was a case-control analysis of 2751 asymptomatic patients without known coronary artery disease enrolled in the Early Identification of Subclinical Atherosclerosis Using Noninvasive Imaging Research registry at Cedars-Sinai Medical Center. A total of 58 patients who subsequently had major cardiac adverse events (MACE; eg, cardiac death, MI, stroke, late revascularization) during 4 years of follow-up constituted the cases and 174 patients without clinical events were sex and propensity matched and served as controls. Noncontrast cardiac computed tomography was performed at baseline; pericardial and total thoracic fat was calculated using automated software, and its relation to MACE was studied.

**Results:** The mean age of cases and controls was 61 years, and 79% were men. There were no significant differences in baseline characteristics between cases and controls except for the Framingham risk score, which was 15 ± 8 in cases and 12 ± 7 in controls. The thoracic fat volume (TFV) and pericardial fat volume (PFV) was higher among cases compared to controls (205 vs 177 cm³ and 102 vs 85 cm³). In multivariate analysis, after adjusting for age, coronary calcification and traditional risk factors, PFV was still significantly associated with MACE (OR, 1.91) as was TFV (OR, 1.81). The association remained strong after adjusting for body mass index, coronary calcium, and Framingham risk score (OR, 1.74 for PFV and 1.78 for TFV). Extrapericardial fat volume (TFV – PFV) was not a predictor of MACE.

**Conclusions:** PFV was significantly higher in a group of asymptomatic patients with intermediate probability of coronary artery disease who suffered MACE compared to patients who did not have MACE.

**Reviewer’s Comments:** It has been shown in the past that pericardial fat is associated with a host of cardiovascular risk predictors. This is the first study that shows that pericardial fat is also independently associated with major cardiac adverse events. Pericardial fat can be calculated from routine noncontract cardiac tomographic scans done for calculation of coronary artery calcium. If proved in larger prospective trials, the addition of PFV to coronary artery calcium scores and the Framingham risk score may improve risk stratification. (Reviewer-Anoop C. Parameswaran, MD).

Keywords: Pericardial Fat, Cardiovascular Events, Tomography

Print Tag: Refer to original journal article
Cardiac Iodine-123 mIBG Uptake Helps Predict Prognosis in Heart Failure

Myocardial Iodine-123 Meta-Iodobenzylguanidine Imaging and Cardiac Events in Heart Failure: Results of the Prospective ADMIRE-HF (AdreView Myocardial Imaging for Risk Evaluation in Heart Failure) study.

Jacobson AF, Senior R, et al:

J Am Coll Cardiol 2010; 55 (May 18): 2212-2221

A low heart/mediastinal ratio of 123I-mIBG predicts an adverse prognosis in patients with heart failure.

Background/Objective: Decreased myocardial uptake of iodine-123 meta-iodobenzylguanidine (123I-mIBG) has been known to be a predictor of adverse outcomes in patients with heart failure. The AdreView Myocardial Imaging for Risk Evaluation in Heart Failure (ADMIRE-HF) study aimed to assess, prospectively, the prognostic value of 123I-mIBG imaging in heart failure.

Participants/Methods: Patients with NYHA functional class II or III with left ventricular ejection fraction (LVEF) ≤35% on optimal medical therapy were studied. Patients were injected with 10 mCi of 123I-mIBG and planar and single-photon emission computed tomography imaging of the thorax was done early (15 minutes) and late (3 hours, 50 minutes), and the heart/mediastinal (H/M) ratios were calculated. Myocardial perfusion imaging with technetium-99m was performed on a separate day. Patients were followed until a 2-year period was up, death occurred, subjects were lost to follow-up, or a set number of cardiac events (heart failure progression, arrhythmias, or cardiac death) occurred.

Results: 961 subjects were included; 80% were male, 66% had ischemic cardiomyopathy, the mean LVEF was 27.1% ± 6.1% and 66% had ischemic cardiomyopathy. During follow-up, 237 (25%) first cardiac events occurred. Twenty-one percent of subjects had H/M ratio ≥1.60, and their risk for cardiac events was significantly lower (HR, 0.40). The 2-year survival was 38% in those with H/M ≥1.6 versus 15% in those with H/M <1.6. The probability of death and all-cause mortality was 11.2% and 16.1%, respectively, for H/M <1.6 versus 1.8% and 3%, respectively, for H/M ≥1.6. The late H/M ratio was independently associated with cardiac events after adjusting for LVEF, functional class, and plasma brain natriuretic peptide (BNP). The H/M ratio was able to provide further risk stratification when added to BNP and LVEF. Nine percent of patients experienced arrhythmic events. This was more common in those with H/M <1.6 (10.4%) versus those with H/M ≥1.6 (3.5%).

Conclusions: Patients with heart failure who have low H/M ratios have a higher incidence of cardiac events. H/M ratio provides predictive power over traditionally used variables such as LVEF, BNP, and functional class.

Reviewer’s Comments: Congestive heart failure is associated with heightened sympathetic activity, increased neuronal release of norepinephrine and subsequent down regulation of cardiac norepinephrine transporter, and desensitization of β-adrenergic receptors. The norepinephrine analogue, 123I-mIBG, can be used to assess cardiac sympathetic nerve activity. In patients with severe heart failure, the late 123I-mIBG uptake is reduced, and the washout rate is higher. Despite smaller studies showing that it has an adverse effect on prognosis, this is the first prospective trial to confirm this. The authors suggest that the finding of a low H/M ratio could enable clinicians to adopt more aggressive measures, such as early adoption of evidence-based therapies such as cardiac resynchronization therapy. (Reviewer-Anoop C. Parameswaran, MD).

Keywords: 123I-mIBG, Prognosis, Heart Failure

Print Tag: Refer to original journal article
Epicardial LV Leads for Biventricular Pacing Have Positive Outcomes

Surgically Placed Left Ventricular Leads Provide Similar Outcomes to Percutaneous Leads in Patients With Failed Coronary Sinus Lead Placement.


Patients with failed percutaneous LV lead placement attempts can benefit from epicardial LV lead placement.

Background: Mounting evidence suggests that cardiac resynchronization therapy (CRT) devices improve the quality of life in patients with congestive heart failure (CHF) and decrease mortality and morbidity. Left ventricular (LV) lead delivery for CRT devices is usually done percutaneously. However, difficult coronary venous anatomy with unsuitable implantation targets at times necessitate epicardial LV lead placement. Such placement is usually performed with a mini-thoracotomy approach but is still considered a significant surgical procedure with certain risks and a longer recovery period compared to the percutaneous approach. It is not well established whether epicardial LV leads provide patients with the same benefits compared to the percutaneous approach.

Objective: To compare the long-term outcomes of patients receiving epicardial LV leads to those with percutaneous leads.

Participants/Methods: Of 452 patients who underwent attempted percutaneous LV lead insertion, 401 (89%) had successful implantations. The other 51 patient procedures failed due to inappropriate targets, high pacing thresholds, or phrenic nerve capture causing diaphragmatic stimulation. Of those, 45 patients were referred for epicardial LV lead placement using an approach of mini-thoracotomy or video-assisted thoracoscopic surgery (VATS). A group of 135 patients with percutaneous leads were selected with propensity matching to be the control group. All patients were followed postoperatively, and their outcomes, mortality, and heart failure status, along with echocardiographic findings, were monitored.

Results: Preoperative demographic and disease parameters were similar between the percutaneous and epicardial LV insertion groups. All patients in the epicardial LV placement group had successful lead placement. Total hospital stay and perioperative complications, including stroke and MI, were similar for both groups. Surgical patients developed acute renal failure (26.0% vs 5.0%) and postoperative infections (12.0% vs 2.4%) more frequently. Thirty-day mortality was similar (2 in surgical patients and 3 in the percutaneous lead group). Mean long-term follow-up was 32 to 39 months. CHF-related admissions, mortality, and long-term improvement in LV ejection fractions were similar in both groups. Significant and similar improvements in NYHA functional class were observed in both groups. This improvement was at least 1 functional class in >60% of surgical patients and >50% of percutaneous patients. LV lead failure occurred in only 1 surgical patient and in 4 percutaneous leads. The percentage of biventricular pacing was similar and excellent in both groups. No significant differences in outcomes or complications were noted between the mini-thoracotomy and the VATS subgroups.

Conclusions: Patients undergoing epicardial LV lead placement following failed percutaneous attempts have similar positive morbidity and mortality outcomes compared to those with successful percutaneous lead placement.

Reviewer’s Comments: At times, percutaneous LV lead positioning is simply not feasible. It is comforting to know that the alternative of epicardial lead positioning gives equal results with no significant increase in complications. (Reviewer-Khalid Almuti, MD).

Keywords: Biventricular Pacemakers, Left Ventricular Leads, Percutaneous Leads

Print Tag: Refer to original journal article
Background: Implantable cardioverter-defibrillators (ICDs) have proven to reduce the incidence of sudden cardiac death in selected populations. Complications such as pneumothorax, cardiac tamponade, lead dislodgement or failure, bleeding, and infection occur in part because of the necessity to place leads in the heart through the vasculature. Vascular anatomy occasionally prevents placement of an ICD.

Objective: To describe the initial experience with an entirely subcutaneous ICD (SQ-ICD) system.

Methods: The SQ-ICD consists of an electrode positioned subcutaneously parallel and 1 to 2 cm leftward of the sternum, connected to a generator positioned over the sixth rib anterior to the mid-axillary line. No fluoroscopy is required for placement. The device can deliver 80-J shocks. Four trials, sponsored by the device manufacturer, were performed from 2001 to 2009. The first trial involved placement of a temporary SQ-ICD, included 78 patients, and aimed to assess optimal electrode configuration. The second trial involved 49 patients and compared the best configuration from trial 1 to a standard transvenous ICD system. The third and fourth trials implanted permanent SQ-ICDs in 6 and 55 patients, respectively. Patients were chosen from the referral population for ICDs and had a class I, IIa, or IIb indication for ICD therapy. Patients with severe renal dysfunction, a need for pacemaker implantation, known ventricular tachycardia <170 bpm or known to terminate successfully with anti-tachycardic pacing were excluded. The primary end point was successful conversion of 2 consecutive induced episodes of ventricular fibrillation.

Results: Trial 1 found that the optimal device placement was as described above. Defibrillation was comparable between the SQ-ICD and transvenous systems in trial 2. All patients who agreed to participate were able to undergo permanent device implantation. The mean ages were 60 and 56 years with ejection fractions of 23% and 34% in trials 3 and 4, respectively. The primary end point was achieved in 98% of patients who received a permanent device. After 46 patient-years of follow-up, 98% of patients were alive. Pocket infections occurred in 2 patients and lead dislodgements requiring reoperation in 4 patients. Twelve episodes of spontaneous ventricular tachycardia were detected and treated successfully.

Conclusions: The SQ-ICD consistently detected and terminated ventricular fibrillation in this small, nonrandomized population.

Reviewer's Comments: ICDs have proven benefit in reducing mortality in select patients. Unfortunately, we have all experienced associated complications with our patients. An alternate approach with lower complications and equal efficacy would be appealing. This interesting paper suggests that an alternative approach may be available in the future. The limited data in these nonrandomized trials suggest reasonable efficacy with avoidance of fluoroscopy but similar procedural times, similar reoperation rates, and without the ability for long-term pacing. Further study with long-term, randomized studies, including patients with more diverse backgrounds and comorbidities, is necessary. (Reviewer-Sumeet K. Mainigi, MD).

Keywords: Implantable Cardioverter-Defibrillator, Subcutaneous Placement

Print Tag: Refer to original journal article
D-Dimer Predicts Future Thromboembolic Risk in AF

Evidence That D-Dimer Levels Predict Subsequent Thromboembolic and Cardiovascular Events in Patients With Atrial Fibrillation During Oral Anticoagulant Therapy.

Sadanaga T, Sadanaga M, Ogawa S:

J Am Coll Cardiol 2010; 55 (May 18): 2225-2231

D-dimer level in patients anticoagulated for atrial fibrillation predicts future cardiovascular events.

**Background:** Levels of D-dimer increase in atrial fibrillation (AF) and can remain high despite adequate anticoagulation.

**Objective:** To assess whether elevated D-dimer levels in patients already anticoagulated for AF would lead to adverse outcomes.

**Participants/Methods:** 269 consecutive patients being treated for AF in a single center were prospectively followed. The relationship between elevated D-dimer levels and adverse outcomes was studied. The end points were thromboembolic events (ischemic stroke, transient ischemic attack, and peripheral embolism) and combined cardiovascular events (thromboembolic events, cerebral hemorrhage, myocardial infarction, and cardiovascular deaths).

**Results:** The mean age of the patients was 74 ± 9 years, and 57% were male; 41% of patients had chronic AF, and the rest had paroxysmal AF. The mean INR level was 1.93 ± 0.53. No relationship was found between INR levels and D-dimer levels. The thromboembolic event rate was 1.8% per year, and the combined cardiovascular event rate was 4.8% per year. The bleeding rate was 1.6% per year. Congestive heart failure, age >75 years, and a history of stroke were predictive of high D-dimer levels (>0.5 μg/mL). Elevated D-dimer was a significant predictor of thromboembolic events. There were 8 events in those with high D-dimer and only 2 events in those with low D-dimer levels. Elevated D-dimer, congestive heart failure, and history of stroke were predictors of thromboembolic events. High D-dimer also predicted combined cardiovascular events including bleeding risk (18 in those with high D-dimer vs 9 in those with low D-dimer levels).

**Conclusions:** Elevated D-dimer levels in those already anticoagulated for AF predict higher risk of future events.

**Reviewer's Comments:** D-dimer is produced due to the formation and lysis of fibrin and is an indicator of coagulation and fibrinolysis. D-dimer levels are increased in AF and decreased with warfarin treatment. In this study, elevated D-dimer levels in treated AF patients predicted future events including thromboembolism. This is a prospective observational study and is hypothesis generating. However, if proven in larger trials, elevated D-dimer levels in patients anticoagulated for AF may help us better refine the risk of future events. Whether increased intensity of anticoagulation in patients with high D-dimer levels should be pursued remains unknown. Of interest, there was an event rate of 1.8% per year in those on warfarin; this is likely higher than expected due to the lower INR goal that was followed (1.5 to 3). (Reviewer-Anoop C. Parameswaran, MD).

**Keywords:** D-Dimer, Atrial Fibrillation, Prognosis

**Print Tag:** Refer to original journal article
New XIENCE V DES Reduces Repeat Revascularization for Ischemia

Everolimus-Eluting Versus Paclitaxel-Eluting Stents in Coronary Artery Disease.

Stone GW, Rizvi A, et al:


After 1 year of clinical follow-up, XIENCE V, a second-generation DES, was found to reduce ischemia-driven target-lesion revascularization compared to the first-generation TAXUS DES.

Background/Objective: Drug-eluting stents (DES) have made a huge impact on the rates of restenosis seen after percutaneous coronary intervention (PCI), However, repeat revascularization procedures and stent thrombosis continue to be problems with room for improvement. Lower-profile stent designs with new polymers and antiproliferative agents are being studied with these problems in mind. The XIENCE V stent is a cobalt-chromium stent with a thin polymer coating that releases a rapamycin analog (such as sirolimus in Cypher stents), everolimus. The XIENCE V stent has been compared to the paclitaxel-eluting TAXUS stent in previous smaller trials, the SPIRIT II and III. These trials demonstrated decreased late-loss (a measure of neointimal proliferation) and non-inferior clinical outcomes with the XIENCE V stent. The SPIRIT IV trial was a larger, randomized, clinical trial that was less restricted in terms of degree of coronary disease and was designed to assess superiority of the XIENCE V stent compared to the TAXUS stent.

Methods: Stable patients with objective evidence of ischemia and non-complex 1- to 3-vessel disease were randomized (2:1) to treatment with either the XIENCE V stent or the TAXUS Express stent. Indefinite aspirin use and clopidogrel for at least 12 months was recommended. Clinical follow-up is expected for up to 5 years. The primary end point was ischemia-driven target-lesion failure, a composite of cardiac death, target-vessel myocardial infarction, and target-lesion revascularization. Subgroup analysis of pre-specified groups was also performed.

Results: From 66 U.S. sites, 3687 patients were randomized to XIENCE V (2458) or TAXUS (1229) stents. At 1-year follow-up, there was a significant decrease in the primary end point in patients treated with XIENCE V versus TAXUS (4.2% vs 6.8%; P =0.001). This was primarily driven by a decrease in target-lesion revascularization (2.5% vs 4.6%; P =0.001). Stent thrombosis at all time points (acute through late) was also significantly reduced with the use of XIENCE V. There was no difference in cardiac death. Of note, all prespecified subgroups with the exception of diabetics benefitted from the XIENCE V stent. Among diabetics, there was no difference in outcomes between the 2 stents.

Conclusions: According to the authors, everolimus-eluting stents, as compared with paclitaxel-eluting stents, resulted in reduced rates of target-lesion failure at 1 year—results that were consistent in all patients except those with diabetes, in whom the results were nonsignificantly different.

Reviewer's Comments: Even after the large advances in PCI initially made by DES, newer-generation DES’ continue to improve on stent-related outcomes in terms of both safety and efficacy (ie, target-lesion failure and stent thrombosis). This study has arguably proven the superiority of the XIENCE V over TAXUS from a clinical standpoint. The lack of advantage of the XIENCE V stent among diabetics, however, demonstrates the arduous challenge of altering the disease process in this group. (Reviewer-Parul B. Patel, MD).

Keywords: Percutaneous Coronary Intervention, Drug-Eluting Stent

Print Tag: Refer to original journal article
Complete revascularization, whether staged or acutely, offers a better prognosis than only infarction-related artery revascularization in patients presenting with STEMI.

**Background:** Primary percutaneous coronary intervention (PCI) is the treatment of choice for patients presenting with an acute ST elevation myocardial infarction (STEMI). Approximately 20% to 40% of patients presenting with acute STEMI have significant disease in a coronary artery other than the infarction-related artery (IRA).

**Objective:** To compare long-term outcomes of 3 strategies: (1) culprit vessel-only revascularization (COR) in which only the IRA is treated with PCI; (2) staged revascularization (SR) in which the IRA is treated in the acute setting and the other vessels are treated electively at a later time; and (3) complete revascularization (CR) in which the IRA and other vessels are treated at the same time.

**Methods:** The authors identified 214 patients who presented with STEMI and multi-vessel disease but who did not have cardiogenic shock, left main disease, prior bypass surgery, or severe valvular disease. Immediately after diagnostic angiography, these patients were randomized to either COR, SR, or CR. The primary end point was a major adverse cardiac event (MACE), defined as cardiac or non-cardiac death, in-hospital death, reinfarction, rehospitalization for acute coronary syndrome (ACS), or repeat unplanned revascularization.

**Results:** At baseline, 214 patients were included in the trial. The mean age was 65.2 ± 12.2 years. Of the 214 patients, 166 (77.5%) were male. There were 84 patients (39.2%) in the COR group, 65 (30.4%) in the SR group, and 65 (30.4%) in the CR group. At baseline, the groups were evenly matched except for slightly more multi-vessel disease in the SR group and more nitrate use in the COR group. The elective procedure in the SR group was performed 56.8 ± 12.9 days after primary PCI. The mean follow-up was 2.5 ± 1.4 years. The rate of MACE was 50% in the COR group versus 20% and 23.1% in the SR and CR groups, respectively. There was a significantly higher incidence of in-hospital death, repeat revascularization, and rehospitalization in the COR group than in the other groups. No significant difference was found in reinfarction and mortality in the 3 groups, although mortality was higher in the COR group. Survival free of MACE and repeat PCI was worse in the COR group than in the SR and CR groups.

**Conclusions:** The incidence of MACE was highest in the COR group. Patients undergoing SR had similar rates of MACE as CR patients.

**Reviewer’s Comments:** This randomized, controlled study of 214 patients shows that complete revascularization, whether at the time of acute STEMI or as a staged procedure, is safe and offers better prognosis than culprit vessel-only revascularization. If confirmed in a larger study, this would change the current practice with attaining complete revascularization as an end point, whether at the index procedure or as a staged procedure. (Reviewer-Pradeep S. Arumugham, MD).
Severe, asymptomatic aortic stenosis does not preclude noncardiac surgery

**Background:** Severe aortic stenosis (AS) is a well-documented predictor of cardiac risk in patients undergoing noncardiac surgery. It is nevertheless unclear as to whether aortic valve surgery should be performed before such surgery in patients with severe but asymptomatic aortic stenosis, since previous studies have provided conflicting data.

**Objective:** “To evaluate the postoperative outcomes of patients with asymptomatic, severe AS who underwent noncardiac surgery.”

**Design:** Retrospective study.

**Participants/Methods:** 30 patients with asymptomatic, severe AS (patients) were compared to 60 age-matched (within 2 years) and gender-matched (ratio, 1:2) patients with mild-to-moderate AS (controls). Patients with symptomatic aortic stenosis or moderate or greater aortic regurgitation were excluded. The primary end point was a composite of death, myocardial infarction, heart failure, ventricular arrhythmias before dismissal, and intraoperative hypotension requiring vasopressor administration.

**Results:** The study population was comprised mainly of men aged >75 years. Patients had an aortic valve area of 0.77 ± 0.16 cm², a mean gradient of 50.1 ± 9.5 mm Hg, and a peak gradient of 84 ± 22 mm Hg. Controls had an aortic valve area of 1.35 ± 0.3 cm², a mean gradient of 19.7 ± 7.42 mm Hg, and a peak gradient of 35 ± 12 mm Hg (P <0.001 for all). The majority of study subjects underwent intermediate-risk surgical procedures similar with respect to the nature of the surgery, type of anesthesia used, and preoperative risk assessment. Combined postoperative events were more common for the patients (n=10; 33%) than for controls (n=14; 23%), but this was not statistically significant (P =0.06). Intraoperative hypotension requiring vasopressor use occurred more often in patients (n=9; 30%) than in controls (n=10; 17%; OR, 2.5; P =0.11). Perioperative myocardial infarction rates were similar for both groups (3%; P =0.74).

**Conclusions:** Intermediate- to low-risk noncardiac surgery for patients with severe, asymptomatic AS can be performed relatively safely. However, intraoperative hypotension may occur frequently.

**Reviewer’s Comments:** Severe AS is a risk factor in patients undergoing noncardiac surgery. The data from previous studies, however, is inconclusive. This is due to numerous studies lacking precision in grading the AS severity, often assessing AS solely on physical findings, as well as studies lacking a control population. Also, there has been a tendency to include both symptomatic and asymptomatic patients in study populations. This study illustrates that noncardiac surgery for certain procedures may be safe. However, most of the subjects in this study population were men, the surgery was predominantly elective and intermediate to low risk, and there may have been a selection bias in the inclusion of a low-risk cohort. As the authors indicate, treadmill testing to further risk stratify these patients and the possibility of percutaneous aortic valve implantation are options to consider. (Reviewer-Suraj Maraj, MD).

**Keywords:** Noncardiac Surgery, Severe Aortic Stenosis, Asymptomatic, Cardiac Risk

**Print Tag:** Refer to original journal article
Nonsteroidal anti-inflammatory drugs increase the risk of acute coronary syndrome.

**Background:** Nonsteroidal anti-inflammatory drugs (NSAIDs) are associated with an increased risk of heart failure and myocardial infarction. The exact pathophysiological mechanism by which NSAIDs increase coronary risk is not well understood.

**Objective:** To quantify the risk for each particular type of acute coronary syndrome (ACS) with the use of NSAIDs. In addition, the effects of NSAID dose and duration, as well as patient characteristics, were assessed.

**Design/Methods:** This was a prospective, multi-center, case-controlled study. Inclusion criteria were a definite diagnosis of ACS, age 40 to 85 years, and the ability to answer a questionnaire. Information on NSAID usage, cardiovascular risk factors, and cardiovascular history was obtained. There was a 1:1 ratio for patients and controls.

**Results:** 2954 patients were hospitalized for ACS at 32 Spanish hospitals. These patients, together with the same number of age-matched controls, answered a structured questionnaire. An adjusted odds ratio (OR) for the particular type of ACS was calculated. The adjusted OR of ACS associated with current use (<7 days before ACS episode onset in patients or date of interview for controls) of NSAIDs was 1.16 (95% CI, 0.95 to 1.42). There was an increased risk in patients consuming high doses (OR, 1.64; 95% CI, 1.06 to 2.53). The risk was also greater in patients with previous ischemic heart disease (IHD) (OR, 1.84; 95% CI, 1.13 to 3.00). Overall, increased risk was due primarily to more non-ST-segment elevation ACS (OR, 1.20; 95% CI, 0.99 to 1.47). NSAIDs did not increase the risk for ST-segment elevation myocardial infarction (OR, 1.00; 95% CI, 0.80 to 1.26). Certain NSAIDs posed a greater risk than others. **Conclusion:** NSAIDs are associated with a small, statistically nonsignificant overall coronary risk. This risk was more apparent for non-ST-segment elevation ACS and was stronger when NSAIDs were used at high doses or in patients with previous IHD.

**Reviewer's Comments:** The use of NSAIDs and cardiovascular risk may be associated with a common mechanism that involves inhibition of cyclooxygenase (COX) 2 enzyme. This article illustrates that NSAID usage may not be associated with a significant risk of ACS in the general population. However, when taken for prolonged periods of time at high dosages and in patients with a history of IHD, there is an increase in the risk of non-ST-segment elevation ACS. Patients with IHD had almost a doubled coronary risk when taking NSAIDs compared to those not on NSAIDs. The study was not powered for subanalysis of each particular type of NSAID and the possible concomitant ACS risk. However, ibuprofen was not associated with an increased risk, although diclofenac was. Both of these drugs differ in their inhibition of the COX-2 enzyme. (Reviewer-Suraj Maraj, MD).

Keywords: NSAIDs, Acute Coronary Syndrome, Type-Specific Risk

Print Tag: Refer to original journal article
The 6-MWT on a treadmill yields results that do not consistently agree with those done in a hallway. Both tests are appropriate, but one or the other should be used for consistency.

**Background:** The 6-minute walking test (6-MWT) is a frequently used test to measure functional capacity and assess the effects of cardiac rehabilitation. The American Thoracic Society guideline recommends the test be done on an indoor flat surface of at least 30 meters; however, treadmills are also used for testing. It is unclear whether the results of either method are interchangeable.

**Objective:** To investigate the interchangeability of results of treadmill and hallway 6-MWT, and to present these results with data on agreement rather than reliability.

**Design:** Pre-experimental design.

**Participants:** 69 patients (61 men; mean age, 61 years; age range, 37 to 81 years) were consecutively selected upon entering cardiac rehabilitation at a university hospital.

**Methods:** The treadmill test was first. Patients did a 3-minute trial walk, rested for 3 minutes, and then did the 6-MWT at 3 km/hr with the ability to adjust speed to their preference. The hallway test was done within 1 week to ensure no functional capacity change. Patients did the 6-MWT on a 44-meter rectangular course at their preferred pace. At the conclusion of each walk, the total distance covered, Borg Fatigue scale rating, heart rate, and oxygen saturation were recorded.

**Results:** Overall walking distances were at least 20% below normative values indicative of compromised functional capacity. Mean walking distance on the treadmill (538 ± 124 m) was slightly less than the hallway (547 ± 103 m), while the Borg rating of perceived exertion was comparable (12.5 vs 12.0, respectively). The mean distance difference was 9 m in favor of the hallway, and the 95% limits of agreement were ± 118 m.

**Conclusions:** The 6-MWT on a treadmill and in a hallway are both practical for cardiac rehabilitation patients. However, results of both tests are not interchangeable because of sizeable individual variability and high disagreement between the 2 tests in terms of distances walked.

**Reviewer's Comments:** Previous reports on the reproducibility of the 6-MWT on a treadmill and in a hallway show that they seem to be similar, but most studies have reported on reliability and not on agreement. These results demonstrate a sizeable discrepancy in the agreement between the 2 tests, even though the authors found no significant differences between mean walking distances in the hallway and treadmill tests. No conclusion can be made regarding which test is easier. There was greater variability in walking distance on the treadmill, which might be due to unfamiliarity with walking on such a device. The authors recommend that cardiac rehabilitation teams should be consistent utilizing the identical 6-MWT for an individual patient at each such assessment. (Reviewer-Debra L. Braverman, MD).

**Keywords:** Cardiac Rehabilitation, 6-Minute Walk Test
Which Test Best Detects CAD in Women With CAD and Hypertension?

Comparison of Exercise Electrocardiography, Technetium-99m Sestamibi Single Photon Emission Computed Tomography, and Dobutamine and Dipyridamole Echocardiography for Detection of Coronary Artery Disease in Hypertensive Women.
Lu C, Lu F, et al:
Am J Cardiol 2010; 105 (May 1): 1254-1260

Dobutamine stress ECG is the best test for detection of CAD in hypertensive women.

Background: The noninvasive diagnosis of epicardial coronary artery disease (CAD) in women with hypertension can be challenging. Women have a lower prevalence of CAD, more single-vessel disease, limited exercise capacity, inappropriate catecholamine release, hormonal influences of estrogen, and anatomic differences. Pathologic changes due to hypertension such as left ventricular hypertrophy (LVH), microvascular impairment, and endothelial dysfunction also make the diagnosis of CAD difficult.

Objective: To evaluate the relative diagnostic ability of exercise electrocardiography (ECG), exercise myocardial perfusion scintigraphy, dobutamine stress echocardiography, and dipyridamole stress echocardiography in hypertensive women who are being evaluated for CAD.

Participants/Methods: 76 hypertensive women who presented for coronary angiography agreed to undergo 4 stress tests: treadmill exercise ECG, exercise MIBI, dobutamine stress echocardiography, and dipyridamole stress echocardiography.

Results: Significant CAD was seen in 31 women (41%); 17 women had single-vessel disease, 11 women had 2-vessel disease, and 3 women had 3-vessel disease. The sensitivity of exercise ECG (81%), MIBI scanning (90%), and dobutamine echocardiography (87%) was similar and was greater than that of dipyridamole echocardiography (61%). The low dipyridamole sensitivity (47%) was due to low sensitivity in patients with single-vessel disease. The sensitivity of all 4 tests was similar in multi-vessel disease. The specificity of exercise ECG (56%) and MIBI scanning (53%) was significantly lower than that for dobutamine (82%) and dipyridamole (91%) echocardiography. Lower specificity of the exercise ECG was found in patients with LVH or ST-T abnormalities at rest. Lower MIBI scan specificity was found in patients with left ventricular hypertrophy (LVH).

Conclusions: The positive predictive value of dobutamine and dipyridamole echocardiography was greater than in exercise ECG and MIBI scanning. Dobutamine stress echocardiography had the greatest overall diagnostic accuracy of the 4 tests. Dipyridamole echocardiography is limited in the detection of mild CAD.

Discussion: The pathophysiology behind the poor diagnostic utility of stress ECG and myocardial scintigraphy in female hypertensive patients is not certain. Female hypertensive patients often have resting ST-T abnormalities. ST depression at peak exercise might result from worsening abnormal repolarization due to rapidly increasing left ventricular wall tension and stress or by ischemia due to LVH, coronary artery endothelial dysfunction, or microvascular impairment rather than obstructive CAD. LVH is a problem for myocardial scanning because of the relative reduction of the microvascular bed due to increased LV mass, compression of intramyocardial vessels by increased external forces, and a reduced cross-sectional area of resistant vessels due to vascular hypertrophy.

Reviewer's Comments: It would have been helpful to compare the results of the 4 different stress test modalities to dipyridamole MIBI in hypertensive women. (Reviewer-Marjorie Stanek, MD).

Keywords: Stress Testing, Women, Coronary Artery Disease, Hypertension

Print Tag: Refer to original journal article
Recurrence of venous thromboembolism is high in patients with an unprovoked first episode.

**Background:** Predicting risk of recurrent venous thromboembolism (VTE) after a first unprovoked episode is important in determining duration of anticoagulation. Current guidelines recommend long-term anticoagulation for all such patients excluding those with isolated calf thrombosis. To date, there is not a reliable risk prediction model that can be applied after a first VTE event.

**Objective:** To develop and test a simple risk prediction model incorporating clinical and laboratory risk markers, and specifically to identify low-risk individuals.

**Participants/Methods:** 929 patients from 4 thrombosis centers were recruited. Subjects were aged >18 years; all were treated with oral anticoagulation ≥3 months following a first unprovoked VTE (deep vein thrombosis [DVT] and/or pulmonary embolism [PE]). Exclusions included proteins C or S deficiency, presence of lupus anticoagulant, patients homozygous for factor V Leiden or the prothrombin mutation, and those who were double heterozygotes. Enrollment commenced with discontinuation of anticoagulation. The primary end point was recurrent symptomatic VTE. A Cox proportional hazards model and a statistical technique called bootstrapping were used to develop and validate a risk prediction tool incorporating both clinical and laboratory variables.

**Results:** Median follow-up was 43.3 months. Symptomatic VTE recurred in 19% (9% in the first year and less subsequently) including 3 fatal PEs. The final prediction model included male sex, proximal DVT, PE, and level of D-dimer. The cumulative probability (95% CI) of recurrence within 5 years was 9.2% (5.4% to 15.5%) in the lowest risk quartile versus 33.1% (25.5% to 42.1%) in the highest risk quartile. The area under the receiver-operating characteristic curve for recurrent events at 12 months was 0.674. Based on these results a simple nomogram chart was developed for estimating risk of recurrent VTE.

**Conclusions:** In this cohort of patients with a first unprovoked episode of VTE, recurrence rate was high, in keeping with previous studies. Current guidelines recommend long-term anticoagulation for most of these patients, yet the majority will not have recurrent events though they will be exposed to the risks of anticoagulation. Using a combination of VTE location, patient's sex, and D-dimer level, a nomogram was developed to distinguish risk categories for recurrence. Women, patients with isolated calf DVT, and patients with low levels of D-dimer all had a low probability of recurrence (as low as 1.9% per year).

**Reviewer's Comments:** This research along with other publications emphasizes the risk of recurrence following first VTE and reveals how little we know about optimal prevention of such recurrence. While more work needs to be done, the authors have given us a good start on how to create a rational approach to patients with this common problem. (Reviewer-Gregg S. Pressman, MD).

**Keywords:** Venous Thromboembolism, Recurrence, Duration of Anticoagulation

**Print Tag:** Refer to original journal article
Complete revascularization results in greater improvement in LVEF compared to incomplete or no revascularization and the degree of improvement can be predicted by dobutamine-cardiac MRI.

Background: When left ventricular dysfunction occurs due to multivessel disease with viable myocardium, revascularization with coronary artery bypass graft surgery (CABG) improves left ventricular ejection fraction (LVEF). Compared to CABG, revascularization of multivessel disease with percutaneous coronary intervention (PCI) when possible, results in comparable survival and myocardial infarction.

Objective: To compare complete and incomplete revascularization by PCI in terms of the impact on LVEF. Assessment of viability and function with cardiac MRI pre- and post-PCI was also performed.

Design/Methods: This was a nonrandomized, observational study of patients with multivessel disease and depressed LVEF. Patients referred for cardiac catheterization were prospectively enrolled if they had at least 2-vessel stable disease and left ventricular wall motion abnormalities. All patients underwent baseline dobutamine-cardiac MRI study as well as delayed-enhancement (DE) cardiac MRI (post-gadolinium). Revascularization with PCI was defined as complete when all significant stenoses were successfully treated and incomplete when at least 1, but not all lesions were treated. Cardiac MRI was repeated post-PCI.

Results: Of 118 patients who met inclusion criteria, 71 completed the study protocol. The mean time interval between initial MRI and PCI was 36 days, and that between PCI and follow-up MRI was 7 months. Complete revascularization occurred in 34 patients, incomplete revascularization in 22 patients, and unsuccessful revascularization in 15 patients. Prior to PCI, baseline cardiac function was similar (LVEF 46% to 49%). After PCI, patients who were completely revascularized had a greater improvement in LVEF (4.2% ± 4.6%) compared to those incompletely (0.7% ± 6.1%) or unsuccessfully (-1.9% ± 4.1%) revascularized. Statistical significance was reached only in comparison to the unsuccessfully revascularized. Dobutamine-cardiac MRI was more sensitive than DE-cardiac MRI in predicting improvement in LVEF post-revascularization.

Conclusions: Complete revascularization for multivessel coronary artery disease improves EF, whereas EF did not change in patients after incomplete or unsuccessful revascularization. Improvement in EF can be predicted by performing cardiac MRI before PCI.

Reviewer’s Comments: In this small observational study, improvement in LVEF seen with complete revascularization with PCI was found to be comparable to that seen in prior CABG studies. Also, this study demonstrated a linear relationship between the extent of dysfunctional (but viable) myocardium and improvement in LVEF post-revascularization. The predictive power of dobutamine-cardiac MRI was greater than that of DE-cardiac MRI as well as that seen in prior studies using echocardiography and nuclear imaging. The results suggest that among patients with multivessel disease and moderately reduced LVEF, assessment with dobutamine-cardiac MRI along with careful assessment of the feasibility of complete revascularization ought to be considered prior to PCI. (Reviewer-Parul B. Patel, MD).

Keywords: Multivessel Coronary Artery Disease, Percutaneous Coronary Intervention

Print Tag: Refer to original journal article
Frequent Atrial Ectopy Increases Stroke Risk

Excessive Supraventricular Ectopic Activity and Increased Risk of Atrial Fibrillation and Stroke.

Binici Z, Intzilakis T, et al:

Circulation 2010; 121 (May 4): 1904-1911

ESVEA in apparently healthy subjects is associated with development of AF and is associated with a poor prognosis in terms of death or stroke.

Background: Supraventricular ectopic complexes (SVEC) are common in acute stroke and transient ischemic attack and may indicate a predisposition to atrial fibrillation (AF).

Objective: To determine the significance of SVEC in relation to risk of stroke, AF, and death.

Participants/Methods: 2969 men and women in Copenhagen, ages 55 to 75 years, were contacted and those with cardiac disease, AF, stroke, cancer, or other life-threatening conditions were excluded. Overall, 678 underwent 48-hour Holter monitoring and were followed-up to 7 years (median, 76 months) for stroke or death (primary end point) and AF. Those with ≥30 SVEC/hour or any runs of ≥20 SVEC were defined as having excessive supraventricular ectopic activity (ESVEA).

Results: 99 subjects had ESVEA. On multivariate logistic regression, age, N-terminal prohormone B-type natriuretic peptide, and systolic/diastolic BP were associated with ESVEA. Stroke/death occurred in 29 of 99 with ESVEA versus 76 of 579 without, yielding a HR of 1.64 (95% CI, 1.03 to 2.60; \( P =0.036 \)) after adjusting for conventional risk factors. SVEC as a continuous variable was also associated with the primary end point. Censoring patients at the time of development of clinical AF did not affect the results. ESVEA was associated with increased risk of AF in Cox regression models, even after adjustment for clinical factors (including blood pressure and body mass index). SVEC was also significantly associated with AF. Further, there was a linear association between frequency of SVEC and incidence of AF, with a 10-fold difference noted between subjects in highest versus lowest frequency SVEC groups (\( P =0.0006 \)).

Conclusions: ESVEA increased risk of stroke/death >60%, and was associated with a 2.7-fold increase in AF. For each 10 SVEC/hour increase, the risk of stroke/death increased 27% while the risk of AF increased 50%.

Reviewer’s Comments: We are all taught that frequent atrial ectopy heralds AF. This population-based study nicely documents that. As the authors point out, SVEC may originate from pulmonary veins, a common source of atrial fibrillation. A critically timed SVEC may act to trigger fibrillatory conduction in the atrium with AF eventually becoming permanent through electrical remodeling and other mechanisms. ESVEA may also be a marker of patients at higher risk of AF or already experiencing undetected paroxysms of the arrhythmia. (Reviewer-Gregg S. Pressman, MD).

Keywords: Supraventricular Ectopy, Atrial Fibrillation, Stroke

Print Tag: Refer to original journal article
Is There a Link Between Exercise BP and Future CVD?

Exercise Blood Pressure and Future Cardiovascular Death in Asymptomatic Individuals.
Weiss SA, Blumenthal RS, et al:

Circulation 2010; 121 (May 18): 2109-2116

Stage 2 Bruce protocol BP >180/90 mm Hg carries 2.4-fold increased risk of CVD death in an asymptomatic nonhypertensive population.

Background: Exaggerated exercise blood pressure (BP) has been associated with higher incidence of future clinical hypertension. However, the correlation of this finding and cardiovascular disease (CVD) has been unclear.

Objective: To evaluate whether exaggerated systolic or diastolic BP attained at low and submaximal exercise is associated with future CVD death.

Design/Methods: This was a prospective cohort follow-up of 6578 asymptomatic patients from the Lipid Research Clinics Prevalence Study. In total, 74% of this population were nonhypertensives (resting BP <140/90 mm Hg). Exercise treadmill Bruce protocol test was performed. Both systolic and diastolic BP were taken at baseline, at stage 2 of Bruce protocol, and at maximal exercise. JNC 7 definition of hypertension was applied to the BP measurements. This population was then followed for 20 years. The primary end point of this study was CVD death.

Results: The mean age of this population was 46 years with 45% of the population being women. There were 385 CVD deaths. The authors found a correlation between the systolic and diastolic BP at rest, Bruce stage 2, and maximal exercise and CVD death. The strongest association of BP and CVD was with the rest BP and Bruce stage 2 BP. However, the significance of this correlation was attenuated once the baseline hypertension status was accounted for. A subgroup of this population, which included the nonhypertensives (BP <140/90 mm Hg), was then further analyzed. In the nonhypertensive population, elevated exercise BP at Bruce stage 2 >180/90 mm Hg was associated with 2.4-fold increased risk of CVD death independent of other risk factors.

Conclusions: Asymptomatic, nonhypertensive individuals with Bruce stage 2 BP of >180/90 are at higher risk for future CVD events.

Reviewer's Comments: In an age when complex blood work and expensive diagnostic tests and therapies are utilized to prevent CVD, a simple BP measurement at submax exercise would be an attractive alternative to identify an asymptomatic population at risk. While stress testing is a common diagnostic tool today, little attention is given to the exercise or hemodynamics portion of the test. This study confirms most of the previous study results regarding the predictive value of rest and exercise BP. Furthermore, it provides a cut-off BP for clinicians to identify their patients at risk and more aggressively risk-stratify them. This study with its impressive follow-up period (>20 years), does have various limitations. As the authors mention, >95% of the study population were white. This study was also originally a lipid study with almost 40% of patients having abnormal lipids. It will be interesting to also report other end points besides CVD death, such as stroke, kidney disease, or development of coronary artery disease. (Reviewer-Behnam Bozorgnia, MD).

Keywords: Exercise, Blood Pressure, Asymptomatic, Future CVD Death

Print Tag: Refer to original journal article
Dual Antiplatelet Agents Increase Bleeding Complication Risk With Device Implantation

Dual Antiplatelet Therapy and Heparin Bridging Significantly Increase the Risk of Bleeding Complications After Pacemaker or Implantable Cardioverter-Defibrillator Device Implantation.

Tompkins C, Cheng A, et al:

J Am Coll Cardiol 2010; 55 (May 25): 2376-2382

Whenever possible, the use of heparin products and dual-antiplatelet agents should be avoided in the PPM and ICD peri-implant period.

Background: Recipients of permanent pacemakers (PPM) and implantable cardioverter defibrillators (ICD) frequently have other cardiovascular comorbidities such as atrial fibrillation and coronary disease with intra-coronary stents or prosthetic heart valves. These comorbidities often dictate the timing and nature of antiplatelet and anticoagulant use in the perioperative device implantation period. Ideally, all these medications would be temporarily withheld to minimize the risk of bleeding complications. However, doing so would place the patient at risk for thromboembolic complications. The optimal strategy for managing anticoagulants and antiplatelet agents during that period remains controversial.

Objective: To assess the risk of bleeding complications with different combinations of antiplatelet and anticoagulant agents.

Design/Methods: This was a retrospective study examining all PPM and ICD recipients at a single center over 3 years. Patients were grouped into 3 major groups: antiplatelet recipients, those on anti-coagulants, and those on neither class of medications. Patients on warfarin were subgrouped based on an international normalized ratio value ≥1.5 or <1.5 at the time of the procedure. Patients receiving "heparin bridging" (unfractionated or low-molecular-weight heparin) were also assessed. The antiplatelet group (ie, use within 5 days of procedure) was subdivided into those on aspirin alone versus dual-antiplatelet agents (aspirin and clopidogrel). The primary end point was a bleeding episode requiring exploration or blood transfusion, or the occurrence of a pocket hematoma necessitating pressure dressing, medication changes, or prolonged hospitalization. Results: The study included 1388 patients with a mean age of 65 years (40% PPM and 60% ICD). There were 71 (5%) bleeding complications that met the study criteria. Hematoma formation accounted for 41 of the cases and need for medication changes accounted for another 17 cases. Four patients required blood transfusions and 5 required pocket exploration. Patients on dual antiplatelet agents were much more likely to have bleeding episodes compared to those not taking antiplatelet agents (7.2% vs 1.6%; P=0.004). A trend toward more bleeding was observed with aspirin alone versus no antiplatelet agents. Warfarin use was associated with a trend toward more bleeding. However, there was no significant difference in the groups with INR ≥1.5 and those <1.5. The use of heparin was associated with a marked increase in bleeding risk. The combination of aspirin and warfarin did not increase bleeding risk compared to warfarin alone. Aspirin with heparin use trended toward more bleeding risk. Use of dual antiplatelet agents or heparin was associated with significant risk factors for bleeding on multivariate analysis.

Conclusions: Significant bleeding complications occur in nearly 5% of device implantation cases. The use of heparin and dual antiplatelet agents significantly increases the risk of these bleeding complications.

Reviewer's Comments: Withholding anticoagulant and antiplatelet agents is easier said than done. Implanters frequently have to bite the bullet and proceed with these agents on board. True patient informed consent is essential in those cases. (Reviewer-Khalid Almuti, MD).

Keywords: Bleeding Complications, Risk, Antiplatelets, Anticoagulants, Pacemakers, Defibrillators

Print Tag: Refer to original journal article
Background: Sudden death or myocardial infarction (MI) is the first presentation of coronary artery disease (CAD) in 60% to 70% of patients. Chronic myocardial ischemia, even in the absence of major events, can lead to congestive heart failure, fibrosis, and arrhythmias. It is possible that asymptomatic CAD patients will have worse prognosis than patients with symptoms. The therapy for asymptomatic CAD is controversial. Freedom from symptoms after percutaneous coronary intervention (PCI) does not guarantee freedom from ischemia.

Objective: To assess the prognosis of patients with asymptomatic CAD after PCI.

Design/Methods: This is a prospective registry study from a single center that included 4592 consecutive patients with CAD, who had undergone elective PCI with a drug-eluting stent from April 2003 to June 2008. From this group, after excluding unstable CAD patients such as STEMI and NSTEMI patients, 1944 patients with stable CAD were identified. There were 1052 asymptomatic patients and 892 patients with stable angina. Primary end point was 1-year all-cause mortality. Secondary end points were death, repeat revascularization, and nonfatal MI. Clinical follow-up was performed at 1, 6, and 12 months. Clinical follow-up data were obtained by telephone interview or office visit.

Results: At baseline, the asymptomatic patients were older, more often men, and more often had chronic kidney disease. Diabetes mellitus was equally prevalent in both groups. Previous MI and coronary artery bypass graft surgery were more common in asymptomatic patients. These patients also had a lower left ventricular ejection fraction. Asymptomatic patients were more likely to have a preprocedure stress test and more likely to have a positive result. The in-hospital adverse events were similar except for a significantly higher incidence of acute renal failure in the asymptomatic group. The asymptomatic patients had a significantly higher 1-year mortality rate (43 [4.1%] vs 16 [1.8%]; \( P =0.003 \)). The incidence of nonfatal MI and target vessel revascularization was similar in the 2 groups. The absence of symptoms and baseline renal insufficiency were strong independent predictors of 1-year mortality.

Conclusions: In patients with stable CAD undergoing elective PCI, the absence of symptoms was associated with an increase in 1-year mortality.

Reviewer’s Comments: The management of asymptomatic CAD is controversial. It may present later with significant cardiac damage, arrhythmias, or acute events. The reason for the lack of symptoms is unknown. Autonomic neuropathy as in diabetes mellitus is one postulated reason. Surprisingly, in this study the presence or absence of symptoms did not correlate with the incidence of diabetes in this group of patients. In this prospective registry study, lack of symptoms was associated with a significant increase in mortality at 1 year. Large randomized prospective studies are needed to answer whether revascularization in this group of patients will improve prognosis. (Reviewer-Pradeep S. Arumugham, MD).

Keywords: Asymptomatic Coronary Artery Disease