N-terminal brain natriuretic peptide is an independent predictor of risk in both the acute and chronic phase after myocardial infarction.

**Background:** Several markers, such as cardiac troponins, N-terminal brain natriuretic peptide (NT-proBNP), C-reactive protein (CRP), and estimated glomerular filtration rate (eGFR), have prognostic value after myocardial infarction (MI). How the prognostic importance of these markers change from the acute phase of MI to the chronic stable phase is not well known.

**Objective:** To evaluate the prognostic value of cardiac troponin I (cTnI), NT-proBNP, CRP, and eGFR during MI, and after 6 weeks and 6 months of clinical stabilization.

**Participants/Methods:** 877 of 3489 patients enrolled in the FRISC (FRagmin and fast revascularization during InStability in Coronary artery disease) II trial had all 4 biomarkers measured at randomization and were included in the trial. These measurements were repeated at 6 weeks and 6 months after randomization. The prognostic value of these biomarkers during 5 years of follow-up was calculated.

**Results:** After a follow-up of 5 years, primary end points of death, MI, and a composite of both occurred in 9%, 17%, and 23%, respectively. NT-proBNP was the strongest predictor of mortality at randomization, and cTnI was predictive of MI and the composite endpoint of death and MI. eGFR and CRP were not independent predictors of events at randomization. During follow-up, NT-proBNP remained the strongest predictor of mortality and acute MI. CRP was predictive of death and MI at 6 months, but cTnI and eGFR provided only limited prognostic information. When added to other clinical variables and risk factors, only NT-proBNP measured at 6 weeks provided incremental prognostic value.

**Conclusions:** Different biomarkers provide different prognostic information over time after MI. NT-proBNP had the strongest prognostic value and provided incremental information over clinical risk factors.

**Reviewer's Comments:** After an episode of acute MI, risk assessment on follow-up is based on conventional clinical risk factors. This study suggests that 6-week measurement of NT-proBNP might be useful to further refine patient risk. Higher NT-proBNP may reflect larger infarct size and more myocardial dysfunction. Surprisingly, although cTnI was a predictor of MI at randomization, it did not independently predict mortality. This may have been because cTnI levels were dichotomized based on the 99th percentile as a prognostic cutoff and not considered as a continuous variable. Also surprising was the lack of association between renal function and prognosis. This was likely due to exclusion of patients with renal dysfunction from the FRISC II study. This small and selected population was randomized 10 years ago, and the results may not be completely applicable in the current era of aggressive medical therapy. (Reviewer-Anoop C. Parameswaran, MD).

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Keywords: Acute Coronary Syndrome, Non-ST-Segment Elevation, Biomarkers, Risk Assessment

Print Tag: Refer to original journal article
Cardiac rehabilitation offers significant survival benefits to all participants, most notably those aged ≥65 years, and should be strongly encouraged in all patients with coronary disease, regardless of age, gender, or socioeconomic status.

**Background:** Older Americans (aged ≥65 years) account for >55% of acute myocardial infarctions and 86% of coronary artery disease deaths. However, most studies that show cardiac rehabilitation (CR) improves survival have been with middle-aged, low- or moderate-risk Caucasian men, and their results may not truthfully indicate outcomes in older varied populations.

**Objective:** To measure consequences of CR on survival in a large cohort of older coronary patients.

**Design:** Observational, retrospective case-controlled study.

**Participants:** 601,099 Medicare beneficiaries aged ≥65 years who were hospitalized in 1997 for cardiac revascularization procedures or coronary disease throughout the United States.

**Methods:** Data were collected from Medicare's National Claims History File, including date of birth, sex, race, date of death when applicable, residence zip code, enrollment status over time, Medicare entitlements, and group health plan membership. Use of CR was defined by Medicare reimbursement for at least 1 session within 1 year following discharge. Statistical analysis was performed using patient sociodemographic characteristics, distance from the patient's residence to the nearest CR facility, health-related characteristics, and socioeconomic characteristics of the patient's zip code. One- to 5-year mortality rates were studied in CR users and nonusers using statistical analytic techniques of instrumental variables, regression modeling, and propensity-based matching.

**Results:** All statistical analyses found a significantly lower 1- and 5-year mortality rate in CR users versus nonusers (P <0.001). Five-year mortality relative reductions were 21% with instrumental variables, 26% with regression modeling, and 34% with propensity-based matching. Only 12.2% (n=73,049) of the cohort used CR. CR users were more likely to be male, younger, white, not on Medicaid, and to have fewer comorbid conditions. Mortality reductions increased progressively with older age and were greater in women than in men in each age group. Average number of sessions for CR participants was 24. Those with ≥25 sessions were 19% relatively less likely to die over 5 years than were matched CR users with ≤24 sessions (P<0.001).

**Conclusions:** In this clinically and socioeconomically diverse older population, mortality rates were 21% to 34% lower in CR users than in nonusers. These results are similar to randomized controlled trials and meta-analyses of CR in younger and more selected populations.

**Reviewer's Comments:** Favorable associations between CR use and survival were found in all race, sex, and age groups and in all clinical subgroups including patients with coexisting congestive heart failure. These results strongly suggest the need to increase use of CR in a broad range of patients who are recovering from acute myocardial infarctions and coronary artery revascularization procedures. (Reviewer-Debra L. Braverman, MD).

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Keywords: Coronary Artery Disease, Survival, Elderly Population

Print Tag: Refer to original journal article
Effect of Beta-Blocker Therapy on Survival in Patients With Severe Aortic Regurgitation: Results From a Cohort of 756 Patients.
Sampat U, Varadarajan P, et al:
J Am Coll Cardiol 2009; 54 (July 28): 452-457

Use of beta-blockers in patients with severe aortic regurgitation may be associated with long-term benefits.

Background: Use of beta-blockers in patients with severe aortic regurgitation (AR) is considered to be a contraindication. This is based on the fact that beta-blockers would prolong diastole and, therefore, allow for a larger regurgitant volume through the aortic valve. However, what if beta-blockers actually decrease the excess beta-adrenergic stimulation created by AR-related volume overload, and if they possibly provide a survival benefit?

Objective: To retrospectively assess the effect of beta-blocker use on outcomes in patients with severe AR.

Methods: The study assessed outcomes of 756 patients with severe AR based on standard echocardiographic criteria. Baseline and follow-up data were obtained from patient records. Patients on beta-blockers had to be on the drug for at least 1 month. Patients on beta-blockers comprised 1 subgroup that was compared to a group not on beta-blockers. The end point of the study was all-cause mortality.

Results: Of patients, 59% were male and mean age was 61 years; mean left ventricular ejection fraction was 54%. Additionally, 14% had diabetes, 65% had hypertension, and 33% had coronary artery disease (CAD). Various beta-blockers were used in 47% of patients. The etiology of AR was bicuspid aortic valve (10%), dilated aortic root (10%), calcific valve disease (30%), endocarditis-related (10%), and unclear or mixed etiologies (40%). There were baseline differences between groups. The beta-blocker group was younger (60 vs 63 years), had more CAD and hypertension, and ended up with aortic valve replacement (AVR) more commonly (49% vs 28%). The beta-blocker group had significantly better survival (average, 4.4 years of follow-up), and it had a 90% and 70% 1-year and 5-year survival rates, respectively. This is compared to 75% and 55% survival at 1 and 5 years, respectively, for the no-beta-blocker group (P < 0.001). Stratification of outcome based on presence of CAD or hypertension showed similar benefits in patients with and without CAD and/or hypertension, suggesting the beta-blocker benefit is independent of any anti-ischemic and/or anti-hypertensive effects. Interestingly, beta-blockers were associated with a survival benefit in those with faster heart rates but not those with slower heart rates. Beneficial effects of beta-blockers were still present even after statistical adjustments for confounders such as age, gender, heart rate, hypertension, CAD, and diabetes among others. The relative risk overall with use of beta-blockers was 0.74 (CI 0.58 to 0.93; P = 0.01).

Conclusions: This study shows that use of beta-blockers in patients with severe AR may be associated with significant survival benefits.

Reviewer's Comments: Beta-blockers were once contraindicated in patients with heart failure. Today, they are among the mainstay therapies for heart failure. Could the same be true for severe AR? Large prospective studies are needed to investigate this issue, but this study provides food for thought. (Reviewer-Khalid Almuti, MD).

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Keywords: Severe Aortic Regurgitation, Long-Term Benefit

Print Tag: Refer to original journal article
Conclusions: The extent of transmural infarction and wall motion abnormalities as determined by comprehensive CMR done after STEMI provides independent prognostic information.

Reviewer's Comments: Clinical risk scores such as TIMI, GRACE, and CADILLAC are traditionally used to predict prognosis after STEMI. Left ventricular systolic function, as determined by echocardiography or nuclear testing, is also a powerful prognostic indicator. For CMR to be a viable clinical tool in assessing prognosis after STEMI, it should provide incremental prognostic value over existing and cheaper risk-stratification methods. In this study, event rates were 23% in those with a large area of transmural necrosis compared with 3% in those without significant transmural necrosis. A similar finding was seen with the extent of wall motion abnormalities. If validated in a larger randomized clinical trial, CMR-derived extent of transmural infarction and wall motion abnormalities could be a promising tool that may provide additional prognostic information over that available from a clinical risk score. (Reviewer-Anoop C. Parameswaran, MD).
A management-based approach to the treatment of infective endocarditis may lead to a dramatic reduction in infective endocarditis-related mortality.

**Background:** Infective endocarditis (IE) has a high in-hospital mortality rate, even though there have been improvements in its medical and surgical management. Multiple medical and surgical specialities are often involved in caring for a patient diagnosed with IE.

**Objective:** To assess the impact of a standardized diagnostic and therapeutic protocol on mortality, as well as to correlate the outcome with compliance with a management-based protocol.

**Design:** Observational before-and-after study.

**Participants:** 333 consecutive patients treated for IE at a referral center from 1991 to 2006.

**Methods:** The study duration was divided into 2 periods: period 1 (1991-2001), before implementation of the therapeutic protocol (n=173); and period 2 (2002-2006), after implementation of the protocol (n=160). The protocol was created following a review of evidence-based studies. It required a consensus from a multidisciplinary task force, including local physicians and surgeons, thus preventing randomization of the study. The protocol included a sampling of biological specimens, use of only 4 standardized antimicrobial agents compared to up to 8 antibiotics with variable dosages as seen in certain guidelines, a standardized duration of treatment, standardized surgical indications, and 1 year of close follow-up.

**Results:** There was a significant reduction in 1-year mortality, ie, 18.5% during period 1 and 8.2% during period 2 ($P=0.008$). Multivariate analysis revealed that management during period 2 was a strong protective factor ($P=0.01$). In addition, there was a statistically significantly better compliance with antimicrobial therapy and fewer cases of renal failure observed during period 2. Also, deaths due to embolic events and multiple organ failure syndrome were significantly decreased during period 2.

**Conclusions:** There was a significant and dramatic reduction in IE-related mortality observed in this before-and-after study, which involved implementation of a management-based approach in treating IE. There were also significant reductions in other comorbidities often associated with IE.

**Reviewer's Comments:** Even in 2009, IE is still a serious and potentially deadly infection. The in-hospital mortality may be as high as 36%. There are numerous medical and surgical professionals who are often involved in taking care of a patient with IE, such that there is often a myriad of different opinions and options as to what the best plan of care is. This may mean deviations from guidelines, which may affect patient prognosis. This paper illustrates how a management-based approach in treating IE may result in dramatic reductions in IE-related mortality and morbidity. It would be interesting to see outcomes to this type of approach at other centers. (Reviewer-Suraj Maraj, MD).

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Keywords: Management-Based Approach, Reduction, Mortality

Print Tag: Refer to original journal article
Exercise training reduces mortality in coronary artery disease patients with high psychosocial stress.

**Background:** Psychosocial stressors, including depression and hostility, are independent risk factors for recurrent myocardial infarction and death in coronary artery disease (CAD) patients. Exercise training, assessed by improved peak oxygen uptake, reduces mortality in CAD patients. Every 1% increase in peak oxygen uptake results in a 2% decrease in cardiovascular death. There remains little data on the potential role exercise may have in modifying depression, hostility, and overall psychosocial stress, which are prevalent in CAD patients. The authors recently reported significant improvements in overall survival after reduction in depression using exercise training.

**Objective:** To evaluate the effects of exercise training on survival in CAD patients with and without psychosocial stress.

**Participants/Methods:** 53 CAD patients with high psychosocial stress were compared to 469 CAD patients with low psychosocial stress. The control group comprised 27 patients with high psychosocial stress, who did not undergo formal cardiac rehabilitation. The Kellner Symptom Questionnaire assessed symptoms of depression, anxiety, somatization, and hostility. Outpatient phase II cardiac rehabilitation exercise training consisted of 12 weeks of 36 educational and exercise sessions.

**Results:** 5-year mortality was 22% in CAD patients with high psychosocial stress versus 5% in those with low psychosocial stress. Exercise training decreased the prevalence of psychosocial stress from 10% to 4%. Mortality in patients who improved exercise capacity of ≥10% (high exercise change) was 60% lower than that in patients with <10% improvement in exercise capacity (low exercise change; 4% vs 10%). Interestingly, while mortality was lower in patients with high psychosocial stress with high exercise change (versus in those with high psychosocial stress with low exercise change), patients with low psychosocial stress with high exercise change had only a trend toward lower mortality than did patients with low psychosocial stress with low exercise change (4% vs 8%; \( P = 0.14 \)).

**Conclusions:** Psychosocial stress is an independent risk factor for CAD patient mortality. Exercise training reduces the prevalence of psychosocial stress, as well as CAD patient mortality. This effect seems to be mediated, at least in part, by beneficial effects of exercise on psychosocial stress.

**Reviewer’s Comments:** This investigation confirms that psychosocial stress is an independent risk factor for cardiovascular mortality, and that exercise training reduces mortality in CAD patients with high psychosocial stress. Interestingly, it seems that improving exercise capacity in patients without psychosocial stress offers less mortality benefit than does it does in patients with high psychosocial stress. This was an observational study with potential selection bias, and patients were not prospectively randomized. Further studies will hopefully confirm the benefit of exercise training in CAD patients with high psychosocial stress. (Reviewer—Vincent M. Figueredo, MD).

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Keywords: Psychosocial Stress, Depression, Hostility, Coronary Artery Disease, Exercise Training

Print Tag: Refer to original journal article
Discretionary glycoprotein IIb/IIIa inhibitor use is safe in select patients pre-treated with thienopyridine and undergoing percutaneous coronary intervention.

**Background:** The Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition With Prasugrel-Thrombolysis in Myocardial Infarction 38 (TRITON-TIMI 38) was a randomized comparison of clopidogrel versus prasugrel, a novel thienopyridine, in higher-risk patients with acute coronary syndromes (ACS) undergoing percutaneous coronary intervention (PCI). Prasugrel treatment was found to reduce cardiovascular death, myocardial infarction (MI), or stroke, but it increased life-threatening and fatal bleeding. Both the benefit and hazard associated with prasugrel treatment were evident by the third day of treatment. Most of the benefit of prasugrel resulted from a reduction in MI. In patients undergoing PCI, glycoprotein (GP) IIb/IIIa inhibitor use also reduced MI.

**Objective:** To look at the impact of GP IIb/IIIa inhibitor use on outcomes in TRITON-TIMI 38.

**Participants/Methods:** Of 13,608 patients randomized, 7414 received a GP IIb/IIIa inhibitor at the interventionalists’ discretion. Patients were treated with a loading dose followed by maintenance therapy of either clopidogrel or prasugrel after the coronary anatomy was known, and no later than 1 hour after PCI. Patients treated with a GP IIb/IIIa inhibitor were more likely to be younger, male, smokers, and to have a history of hypercholesterolemia. They were also more likely to be in North America and to undergo multi-vessel PCI.

**Results:** GP IIb/IIIa inhibitor use did not affect the efficacy or safety outcome differences between patients treated with clopidogrel versus prasugrel. Prasugrel treatment reduced MI regardless of whether a GP IIb/IIIa inhibitor was used. The overall incidence of MI was not affected by GP IIb/IIIa inhibitor use. Prasugrel treatment increased bleeding risk regardless of GPIIb/IIIa inhibitor use. The overall risk of bleeding in the 2 arms combined was similarly not affected by GP II/IIIa inhibitor use.

**Reviewer’s Comments:** GP IIb/IIIa inhibitor use did not impact outcomes in the 2 arms combined, nor did it affect differences in outcomes between patients treated with clopidogrel versus prasugrel. This finding should be interpreted with caution, as GP IIb/IIIa inhibitor use was not randomized. Certain baseline and procedural characteristics increased the interventionalists’ likelihood of its use. It is possible that selective GP IIb/IIIa inhibitor use was appropriate, thus exerting an overall neutral effect on both ischemic and hemorrhagic outcomes, and not affecting observed differences between prasugrel and clopidogrel. It is not clear whether outcomes would be different if the higher (600-mg) loading dose of clopidogrel (faster onset of action) was to be given (vs 300-mg dose). Most catheterization labs today probably prefer to administer 600 mg. According to the American College of Cardiology, among patients pre-treated with a thienopyridine, GP IIb/IIIa inhibitor use during PCI in ACS is considered “reasonable” (class IIa). The results of this study do not challenge this recommendation but confirm that GP IIb/IIIa inhibitors may be administered without additional hazard in select patients pre-treated with a thienopyridine. (Reviewer-Parul B. Patel, MD).

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Keywords: Acute Coronary Syndrome, Antiplatelet Therapy, Percutaneous Coronary Intervention

Print Tag: Refer to original journal article
Myocardial Bridge May Promote Proximal Atherosclerosis

Anatomic Properties of Myocardial Bridge Predisposing to Myocardial Infarction.

Ishikawa Y, Akasaka Y, et al:

Circulation 2009; 120 (August 4): 376-383

Even though atherosclerosis is reduced beneath it, a myocardial bridge may promote more proximal atherosclerosis.

Background: A "myocardial bridge" (MB) is a band of myocardium covering a coronary artery, usually the left anterior descending (LAD) artery. It is frequent on autopsy (>50%) but much less common on coronary angiography (<5%). While it causes systolic constriction, it is considered benign since coronary flow is mostly diastolic. Recent reports have suggested that an MB may modulate atherosclerosis in segments proximal to it.

Objective: To assess the effect of an MB on myocardial infarction (MI) occurrence.

Design: Pathological study involving 100 autopsied hearts containing an LAD infarct (MI), 100 hearts with an MB of the LAD but no MI, and 100 hearts with neither.

Methods: The LAD, from coronary ostium to apex, was removed and sectioned every 5 mm. Severity of atherosclerosis was estimated by intimal to medial ratio. Length of the MB was estimated by number of sections involved; thickness was measured microscopically, and an "MB muscle index" (MMI) was generated by multiplying the 2. Four groups were analyzed based on presence/absence of MI and presence/absence of MB.

Results: 46 MI hearts had an MB. These were younger, although this did not reach statistical significance. Hypertension and hypercholesterolemia were more common in these patients, and heart weights were greater. When present, thickness and MMI of an MB were greater in those with MI (P =0.048 and P =0.039, respectively). In the MI(+)MB(+) group, intima-media ratio was greater in the first centimeter from the coronary ostium versus the MI(+)MB(-) group. In the MI(+)MB(+) group, intima-media ratio was significantly decreased beneath the MB compared with proximal segments, which was also the case in the MI(-)MB(+) group.

Location of the MB and the coronary segment with greatest intima-media ratio was correlated, especially in the MI(+)MB(+) group. When comparing the 2 MB groups, an aggregation of severe stenotic lesions was noted 2 cm from the MB entrance in the MI(+)MB(+) group.

Conclusions: Severity of atherosclerosis was less beneath an MB. However, an MB seemed to predispose to MI through increased proximal LAD atherosclerosis. Thus, it appears that an MB can decrease the severity of atherosclerotic disease beneath it while increasing the severity of disease proximal to it.

Reviewer's Comments: MB is typically dismissed as interesting but ultimately unimportant. Because most coronary flow is diastolic, systolic vessel constriction is considered benign in most cases. This work challenges that assumption by noting that MB may alter the natural history of coronary atherosclerosis. Further, the authors and the accompanying editorial point out that detection of an MB, while relatively uncommon at catheterization, may be substantially increased when cardiac CT imaging is used. As with all cases where traditional ideas and concepts are challenged, this work has the potential to lead us in new directions in our understanding of pathophysiology and how clinical disease develops. (Reviewer-Gregg S. Pressman, MD).

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Keywords: Myocardial Bridge, Left Anterior Descending Artery, Atherosclerosis

Print Tag: Refer to original journal article
Background: Atrial fibrillation (AF) is expected to reach epidemic proportions in the next few decades. New medications and catheter-based ablation procedures offer promise but have not been proven to reduce stroke risk. Many individuals qualifying for chronic anticoagulation do not receive it because of safety concerns or intolerance. The WATCHMAN device is a self-expanding, nitinol, umbrella-like device undergoing study for percutaneous closure of the left atrial appendage (LAA).

Objective: To demonstrate that percutaneous LAA closure in patients with AF is non-inferior to warfarin treatment alone.

Participants/Methods: Patients with paroxysmal, persistent, or permanent AF with a CHADS2 score of ≥1 were randomized to the control arm (warfarin alone; n=244) or to the intervention arm (percutaneous closure of the LAA using the WATCHMAN device; n=463). Patients were excluded if they could not take warfarin, had other comorbidities that required warfarin, a known LAA clot, symptomatic carotid disease, mobile aortic atheroma, or right-to-left cardiac shunt. After closure, warfarin was used for 45 days, and transesophageal echocardiography (TEE) was performed at 45 days, 6 months, and 12 months to assess stability and closure. Clopidogrel and aspirin were taken from 45 days to 6 months, then aspirin indefinitely.

Results: The WATCHMAN device was successfully implanted in 88% of patients. At 45-day and 6-month follow-up, 86% and 92% of patients, respectively, had appropriate closure on TEE and discontinued warfarin. A therapeutic international normalized ratio (INR) was maintained in the control group 66% of the time. The primary composite efficacy end point (stroke, cardiovascular or unexplained death, or embolism) was 3.0/100.0 patient-years in the closure group and 4.9/100.0 patient-years in the control group (rate ratio, 0.62). The probability of non-inferiority was >99.9%. At 2 years, the cumulative event rate was 5.9% in the closure group and 8.3% in the control group. Periprocedural ischemic strokes occurred in 5 patients in the closure group, mainly due to air emboli, 2 of whom subsequently died. Hemorrhagic strokes occurred less frequently in the closure group. Significant pericardial effusion occurred in 4.8% of closure patients, although the incidence decreased with operator experience. The closure device embolized in 3 patients; 2 required surgical removal.

Conclusions: Percutaneous LAA closure appears non-inferior to standard warfarin therapy.

Reviewer's Comments: Warfarin has historically been the Achilles heel of AF management. In this study, therapeutic INR was achieved only 66% of the time. Percutaneous LAA closure appears promising as adjunctive therapy for AF management. However, it is unknown whether closure is an option for patients who cannot tolerate even a short course of warfarin. Serious procedure-related complications occurred, although they improved with operator experience. Limitation of this technique to more-experienced centers would likely be advised if it proves to be appropriate therapy. (Reviewer-Sumeet K. Mainigi, MD).

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Keywords: Atrial Fibrillation, Stroke, Left Atrial Appendage

Print Tag: Refer to original journal article
AFib Precipitated by Alcohol, Illicit Drug Use in Young Adults

Alcohol and Illicit Drug Use as Precipitants of Atrial Fibrillation in Young Adults: A Case Series and Literature Review.

Krishnamoorthy S, Lip GYH, Lane DA:
Am J Med 2009; 122 (September): 851-856

Alcohol and illicit drugs are arrhythmogenic and are associated with atrial fibrillation in young adults.

**Background:** Atrial fibrillation (AF) occurs infrequently in young patients (aged ≤45 years). Acute alcohol consumption and binge drinking have been associated with new-onset AF. There is limited literature on the association between new-onset AF and illicit drug abuse. There are no clear guidelines on treatment of AF in patients presenting with "lone" AF precipitated by alcohol or illicit drugs apart from avoidance of the precipitant, and there exist differences in the "real-life" management of such patients.

**Objective:** To analyze the association between alcohol and illicit drug use and AF in young adults.

**Methods:** The authors retrospectively analyzed young (defined as ≤45 years) patients with "lone" AF who were admitted to the hospital with an ECG-confirmed diagnosis of AF or atrial flutter, precipitated by either alcohol or illicit drugs, over a 6-year period.

**Results:** The study included 88 patients aged ≤45 years who were admitted with AF or atrial flutter. In 22 patients (25%), alcohol (n=19) and/or illicit drugs (n=3) were found to be the precipitant. Of patients, 1 required electrical cardioversion, and the rest cardioverted back to sinus rhythm either pharmacologically or spontaneously. All antiarrhythmic (AA) drugs were well tolerated with variable success rates: flecainide, (n=6, 100%) verapamil, (n=3, 100%), beta-blockers, (n=6, 86%), and amiodarone, (n=3, 33%). Twelve patients were investigated for AF burden by 24-hour Holter monitoring, and the majority also underwent a transthoracic echocardiogram. One patient presented with stroke. At discharge, 14 patients were treated with AA drugs, and 10 received either antiplatelets or anticoagulants. Most patients were followed up for at least 12 months, during which time 6 had further paroxysms, all of whom continued to abuse either alcohol (n=5) or illicit drugs (n=1).

**Conclusions:** Alcohol and illicit drugs are arrhythmogenic and are associated with AF in young patients.

**Reviewer's Comments:** This study discusses an interesting topic, that of alcohol and drug use and the association with AF in young adults. The predominant precipitant of AF in this case series was alcohol (86%), followed by marijuana (13%) and cocaine (4%). Optimal management of these patients and long-term effects of these substances on the heart and AF recurrences are still unclear. The authors contend that beta-blockers may be the ideal drug of choice in these patients, as initiation of AF in most cases is from a hyperadrenergic state, and they advise avoiding them in cases of cocaine, opiate, or amphetamine abuse. Some limitations of the study include being a retrospective study and having a small sample size. Patients who had paroxysms in this study continued to abuse alcohol and drugs. Long-term follow-up data are needed to confirm whether AF paroxysms are related to continued abuse of alcohol and illicit drugs. (Reviewer-Sahil Mehta, MD).

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Keywords: Atrial Fibrillation, Alcohol, Illicit Drug Use, Young Adults

Print Tag: Refer to original journal article
Active commuting is positively associated with fitness in men and women and inversely associated with BMI, obesity, triglyceride levels, blood pressure, and insulin level in men.

**Background:** Walking is a popular leisure-time physical activity. However, not much is known about active commuting (walking or biking to work), and its possible association with obesity, fitness, and cardiovascular disease (CVD) risk factors.

**Design/Methods:** The Coronary Artery Risk Development in Young Adults (CARDIA) study is a population-based prospective epidemiologic study that examines determinants and progression of CVD risk factors in the young adult population. There were 2364 participants enrolled in the CARDIA study who worked outside the home during year 20 of the study (2005 and 2006). These were the patients included in this cross-sectional study. Associations between walking or biking to work (self-reported time, distance, and mode of commuting) with body weight, obesity (body mass index [BMI], ≥30), fitness (symptom-limited exercise stress testing), and objective physical activity (accelerometry) were analyzed by sex-stratified regression modeling. The association between active commuting and CVD risk factors, including blood pressure and serum levels of fasting lipids, glucose, and insulin, was also similarly assessed.

**Results:** There were 16.7% of participants who used any means of active commuting to work. After controlling for multiple factors, such as physical activity index excluding walking, men with any form of active commuting (as compared to no active commuting) had a reduced likelihood of obesity, reduced CVD risk, (by comparison of triglyceride levels, mean fasting insulin levels, and mean diastolic blood pressures), and higher fitness levels. Women displayed only the positive association between active commuting and higher fitness levels.

**Conclusions:** Active commuting has a positive association with fitness in both men and women. In men, it is also inversely associated with BMI, obesity, triglyceride levels, blood pressure, and insulin levels. Active commuting should be investigated as a modality for maintaining or improving health.

**Reviewer’s Comments:** Walking is a simple and cheap form of leisure-time physical activity. It is also an integral component of various physical activity guidelines in promoting cardiovascular health and maintaining optimal body weight. This study, although cross-sectional and observational in nature, raises the possibility that actively commuting to work may result in significant benefits in reducing various cardiovascular disease risk factors in men. A lack of this beneficial association with women may be due to women having a lower intensity of activity during active commuting. However, there is a positive association with fitness levels in both men and women. (Reviewer-Suraj Maraj, MD).

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Keywords: Active Commuting, Fitness, Cardiovascular Disease Risk Factors, Positive Association

Print Tag: Refer to original journal article
Background: Stent diameter, stent strut thickness, and type of CT technology used have been seen to influence the assessibility of stents and detection of in-stent stenosis. Dual-source CT (DSCT) provides higher temporal resolution compared with previous scanner generations that may allow more accurate evaluation of coronary stents.

Objective: To evaluate the accuracy of DSCT for assessment of coronary artery in-stent restenosis.

Participants/Methods: This study looked at 112 patients with 150 previously implanted coronary stents (diameter ≥3.0 mm) who were examined using DSCT before conventional coronary angiography. Patients with impaired renal function, acute coronary syndrome, in non-sinus rhythm and possible pregnancy were not included. Stent-specific exclusions were all lesions with >1 implanted stent and stents implanted in bypass grafts. Stents were classified as assessable or not assessable. All assessable stents were further classified for absence or presence of in-stent restenosis (>50% diameter reduction) using DSCT, and results were compared with those using quantitative coronary angiography.

Results: The authors determined that, "mean stent diameter was 3.27 ± 0.35 mm. Fifteen of 80 stents (19%) with a diameter of 3.0 mm were not assessable, and all 70 stents >3.0 mm were assessable." DSCT correctly identified 16 of 19 in-stent restenoses in 135 assessable stents, as well as the absence of in-stent restenosis in 110 of 116 stents (sensitivity 84%, specificity 95%, positive-predictive value [PPV] 73%, and negative-predictive value 97% in assessable stents). Heart rate showed no significant effect on the rate of assessable stents. After adjustment for patient demographics and strut thickness, stent diameter remained significantly associated with stent assessibility in multivariate analyses. However, diagnostic accuracy in assessable stents was not significantly dependent on stent diameter.

Conclusions: DSCT may be useful to noninvasively detect in-stent restenosis, especially in stents with a relatively large diameter.

Reviewer's Comments: In my opinion, this was a very well-conducted study. The authors found that the PPV (73% for all assessable stents) using DSCT was higher than reported in most previous studies that used 16- to 64-slice CT for evaluation of in-stent restenosis. Some limitations of this study include a low rate of significant in-stent restenosis (19 of 150 stents), leading to wide confidence intervals in sensitivities and PPVs. Visual estimation and stent diameter reduction >50% were used for the definition of significant in-stent restenosis compared with late lumen loss and other techniques that define and quantify in-stent restenosis, and included single stents only, whereas overlapping, consecutive, bifurcation, or bypass stents were excluded from evaluation. DSCT seems to be a useful tool to noninvasively detect in-stent restenosis in stents with a relatively large diameter. Future studies with large sample sizes are needed to further this fact. (Reviewer-Sahil Mehta, MD).

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Keywords: Coronary Artery, In-Stent Restenosis, Dual-Source CT

Print Tag: Refer to original journal article
A low number of patients elect to continue outpatient cardiac rehabilitation after inpatient cardiac rehabilitation following acute coronary syndrome.

**Background:** It has been reported that only 17% to 41% of appropriate cardiac rehabilitation patients attend such programs, and 40% to 50% of participants drop out of long-term outpatient programs.

**Objective:** To analyze differences between patients who continue outpatient rehabilitation (OutCR) after inpatient cardiac rehabilitation (InCR) versus those who do not, and which factors influence their decisions.

**Design:** Observational cohort study.

**Participants:** 72 patients (19 women; mean age 57 ± 9.4 years) in InCR 2 to 3 weeks after acute coronary syndrome (ACS) treated with percutaneous coronary intervention. All patients had an exercise tolerance of ≥3 MET, no significant ST changes up to 5 METS, no serious arrhythmias, and an ejection fraction >35%.

**Methods:** Admission and discharge assessments of the following were made: comorbidities, employment, economic status, education, marital status, place of living, smoking status, quality of life, and psychological status. On discharge, patients were advised to begin 12-week OutCR consisting of exercise sessions 2 to 3 times per week. If a patient refused, they were asked to explain.

**Results:** 2 men discontinued InCR due to medical complications. Of 70 patients who completed InCR, 16 (23%) attended and completed OutCR. At baseline, patients who proceeded to OutCR had lower scores for emotional stress (4.4 ± 1.09 vs 5.3 ± 1.34; \( P = 0.02 \)), depression (12% vs 39%; \( P = 0.05 \)), and anxiety (3.1 ± 1.75 vs 4.4 ± 2.12; \( P = 0.04 \)). After completing InCR, those who proceeded to OutCR had lower scores for emotional stress (3.8 ± 1.51 vs. 4.8 ± 1.4; \( P = 0.03 \)) and higher scores for mood (7.7 ± 1.25 vs 6.7 ± 1.69; \( P = 0.04 \)). There was a significant difference in smoking (OutCR participants were less likely to smoke; \( P = 0.05 \)) and employment (OutCR participants were more likely to have a job; \( P = 0.03 \)), but no differences in other demographic data. More than 80% of patients preferred InCR, citing convenience and continuous medical care as the reasons. The most frequent perceived barriers to OutCR were conflict with work and commuting problems.

**Conclusions:** A low number of patients elect to continue OutCR after InCR following ACS. Primary factors that influence this decision were psychological status, smoking status, and employment. Work conflicts and commuting problems were the most prominent barriers to OutCR. The main advantages to InCR were the convenience and constant medical supervision.

**Reviewer's Comments:** It appears that high patient motivation is required for participation in OutCR. Patients with lower mood and higher levels of anxiety should be especially encouraged to go to OutCR, as in addition to the cardiovascular benefits, there is an opportunity to apply psychotherapy in the comprehensive program. (Reviewer-Debra L. Braverman, MD).

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Keywords: Acute Coronary Syndromes, Inpatient, Outpatient, Determinants

Print Tag: Refer to original journal article
Statin Reload Cardioprotective During PCI

Efficacy of Atorvastatin Reload in Patients on Chronic Statin Therapy Undergoing Percutaneous Coronary Intervention: Results of the ARMYDA-RECAPTURE Randomized Trial.


J Am Coll Cardiol 2009; 54 (August 4): 558-565

Reloading patients on chronic statin therapy prior to percutaneous coronary intervention may reduce the likelihood of periprocedural infarct.

**Background:** Prior randomized studies have demonstrated the protective effect of statin pretreatment prior to percutaneous coronary intervention (PCI) in the setting of chronic stable angina as well as acute coronary syndrome (ACS). The benefit was driven by a reduction in periprocedural myocardial infarction (MI). Prior studies looked at statin-naïve patients. Given the large number of patients referred for cardiac catheterization on chronic statin therapy, one wonders whether reloading with statin prior to the procedure might also be cardioprotective.

**Objective:** To determine whether reload with atorvastatin would be protective in patients on chronic statin therapy undergoing PCI.

**Participants/Methods:** 383 patients from 4 Italian centers were randomized to atorvastatin load, 80 mg, 12 hours prior to the procedure and another 40 mg 2 hours prior to the procedure or placebo. All patients were treated with atorvastatin 40 mg daily post-procedure. Although ACS patients were included, those requiring emergent angiography (<2 hours) were excluded. Cardiac enzymes were drawn prior to and at 8 and 24 hours after PCI. The primary end point was 30-day major adverse coronary events (MACEs; cardiac death, MI, or target vessel revascularization). Subgroup analysis of MACEs in ACS versus stable patients was a prespecified secondary end point.

**Results:** The primary end point was reached in 3.7% of the treatment group and in 9.4% of the placebo group (P = 0.037). All MACEs were due to MI except in 1 case of death in the placebo group. There was no elevation of liver enzymes after statin treatment, and there were no cases of statin discontinuation due to intolerance. In the approximately 46% of ACS patients, there was a significant benefit with reload (MACE 3.3% vs 14.8% in placebo group; P = 0.015) that was not seen in stable patients (4.0% vs 4.9% in placebo group; P = 0.98).

**Reviewer's Comments:**

**Conclusions/Reviewer's Comments:** The cardioprotective effect of acute statin pretreatment prior to PCI can likely be attributed to its attenuation of the response to injury and inflammation and, possibly, an antithrombotic effect. As discussed by the authors and an accompanying editorial, these pleiotropic effects of statin therapy are lost over time, and the benefit of a reload has been demonstrated in animal models of ischemia. ACS patients with breakthrough inflammation may benefit from a statin reload, possibly more so than stable patients undergoing PCI. The authors also discuss the possible role of a dose-dependent effect on inflammation and platelet activation seen in prior studies. In conclusion, statin-naïve patients undergoing PCI should be treated prior to the procedure. Although this was a small study, the evidence here suggests that patients with ACS on chronic statin therapy ought to be reloaded prior to PCI. Perhaps early reload should be studied in all ACS patients, and also in patients with or at risk for acute cerebral ischemia, such as those undergoing carotid stenting. (Reviewer-Parul B. Patel, MD).

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Keywords: Statins, Percutaneous Coronary Intervention, Acute Coronary Syndrome

Print Tag: Refer to original journal article
Exercise training can reduce risk factors for coronary artery disease and improve glycemic control in type 2 diabetes mellitus and should therefore be encouraged.

**Background:** Type 2 diabetes mellitus (T2DM) can lead to cardiovascular complications responsible for 70% of the deaths due to T2DM. Exercise training has important effects on development of complications in T2DM.

**Objective:** To document mechanisms whereby exercise helps manage T2DM, to analyze the evidence, to provide practical guidelines for exercise training programs and safety issues, and to review guidelines for initiating an exercise program.

**Design/Methods:** A review of randomized controlled trials that assessed the effect of exercise on metabolic control and vascular structure and function in T2DM was performed.

**Results:** Exercise has favorable metabolic effects (glycemic control, weight loss) and favorable effects on risk factors (lipids and hypertension). There are also direct vascular effects (endothelial dysfunction and vascular distensibility). The effect on HbA1c is modest, but can produce a clinically significant improvement. Exercise training can also improve insulin sensitivity/resistance and reduce hyperglycemia-related medications. Endurance training reduces visceral fat. The extent of benefit in the reduction of coronary artery disease (CAD) is still to be determined. For patients who wish to do a low-to-moderate exercise intensity program, a stress test should not be necessary in the absence of high-risk clinical or ECG features. A stress test may be recommended for a patient with known CAD if there is a change in clinical status or no recent stress test for <2 years. If no CAD, a stress test could be recommended for symptoms, suspected CAD with clinical findings of peripheral artery disease or cerebrovascular disease, with ECG findings of infarction or ischemia, or if a vigorous exercise program is planned. Insulin dosages or diet may need adjustment to avoid hypoglycemia. Patients should minimize foot trauma, particularly in the presence of peripheral vascular disease. If proliferative retinopathy is present, patients should avoid anaerobic exercise that involves a valsalva maneuver. Those with severe peripheral neuropathy should avoid weight-bearing exercise. Patients should accumulate a minimum of 150 minutes/week of at least moderate-intensity physical activity and/or 90 minutes/week of at least vigorous-intensity exercise. Resistance training at least 3 times per week should be encouraged. In patients with deconditioning and limited flexibility, shorter, more frequent periods of brisk activity may be better tolerated (10 minutes). Sedentary individuals should initiate activity at a lower level. Patients should be educated about symptoms of myocardial ischemia. Use of large muscle masses such as with cycling and walking are best. Swimming can minimize the limitations to exercise in patients who are obese or have poor foot care.

**Conclusions:** Exercise training should be encouraged in T2DM patients.

**Reviewer's Comments:** Exercise training can reduce risk factors for CAD in T2DM and improve glycemic control. Although clinical outcomes are yet to be defined, exercise training should be encouraged in this population. (Reviewer-Marjorie Stanek, MD).

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Keywords: Exercise Training, Diabetes Mellitus, Cardiovascular Risk

Print Tag: Refer to original journal article
By delivering paclitaxel on an angioplasty balloon, problems associated with drug-eluting stents might be avoided.

**Background:** Drug-eluting stents are now standard of care in most percutaneous coronary interventions. However, there is a small risk of late and very late stent thrombosis. Drug-coated balloon catheters represent an alternative that might effectively reduce restenosis without incurring the risk of late/very late stent thrombosis.

**Participants/Methods:** 130 patients with single restenosis in a bare metal stent were enrolled. Patients with unstable coronary syndromes, glomerular filtration rate <30 mL/minute or life expectancy <2 years were excluded. Angiographic exclusion criteria were stented segments >22.0 mm in length, vessel diameters <2.5 mm, stenoses <70% luminal diameter, unprotected left main stenosis, or stents covering a side branch >2.0 mm. Subjects were randomized to a paclitaxel eluting stent (Taxus Liberté, Boston Scientific) or coronary angioplasty with a paclitaxel-coated balloon catheter. All received ≥100 mg aspirin/day indefinitely. Clopidogrel 75 mg/day was given for 3 months after balloon angioplasty and 6 months after stent implantation. Late lumen loss at 6 months by quantitative coronary angiography was the primary end point. Secondary end points were restenosis, target-lesion revascularization, stent thrombosis, myocardial infarction, and death at 12 months.

**Results:** Most subjects were men; mean age in both groups was 65 years. Most had multivessel disease and the pattern of restenosis was predominantly diffuse. Analysis was by intention to treat. Five patients in the balloon group required stents for treatment of iatrogenic coronary dissection. In total, 116 patients (89%) had angiographic follow-up at 6 months; 3 died and 12 declined angiography. Mean late lumen loss was 0.38 ± 0.61 mm in the stented group and 0.17 ± 0.42 mm in the balloon-treated group (P = 0.03). Restenosis occurred in 12 of 59 patients (20%) in the stented group and 4 of 57 patients (7%) in the balloon group (P = 0.06). Clinical end points at 12 months occurred in 22% of the stented group versus 9% of the balloon-treated group (P = 0.08). As-treated analysis did not change the results. Stent thrombosis did not occur.

**Conclusions:** Drug-coated balloon angioplasty resulted in less late lumen loss than drug-eluting stent placement in patients with in-stent restenosis. This advantage occurred despite only 3 months of dual antiplatelet therapy in the balloon group.

**Reviewer's Comments:** Drug-eluting stents have largely solved the problem of restenosis, but at the cost of late/very late stent thrombosis—a potentially disastrous complication. This is probably related to delayed endothelialization of the stent struts due to prolonged delivery of drugs at high dosage. By use of a drug-coated balloon, this problem is avoided as the drug is delivered more uniformly and for a brief period of time. This technique also avoids the potential problem of an inflammatory reaction induced by the polymer used to adhere the drug to the stent. (Reviewer-Gregg S. Pressman, MD).

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Keywords: Paclitaxel-Coated Balloon, Stent, In-Stent Restenosis

Print Tag: Refer to original journal article
Potential Antiarrhythmic Effects of the Aldosterone Antagonist Eplerenone

Aldosterone Blockade Attenuates Development of an Electrophysiological Substrate Associated With Ventricular Tachyarrhythmias in Heart Failure.

Stambler BS, Laurita KR, et al:

Heart Rhythm 2009; 6 (June): 776-783

Aldosterone antagonists may prevent adverse electrical remodeling from occurring in heart failure patients.

Background: Patients with left ventricular (LV) dysfunction and consequent chronic heart failure (CHF) are at risk for life-threatening ventricular arrhythmias (VA) that can result in considerable morbidity and mortality. The electrophysiologic substrate for such arrhythmias results from alterations in conduction, repolarization, and myocyte refractoriness. Abnormal levels of aldosterone in CHF patients are known to contribute to arrhythmogenesis. Aldosterone blockers (AB) have been shown to reduce the risk of sudden cardiac death in these patients. The mechanisms for this benefit are poorly understood.

Objective: To investigate whether the AB agent eplerenone protects against life-threatening VAs by preventing or reversing the detrimental electrical remodeling effects in an animal heart failure model.

Methods: The study used a dog model of heart failure induced with rapid ventricular pacing (RVP). Thirty-five dogs were divided into the following groups: (1) placebo + no RVP; (2) eplerenone + no RVP; (3) placebo + RVP; and (4) eplerenone + RVP. Each group had between 6 and 11 dogs. Groups 3 and 4 underwent rapid ventricular pacing to induce heart failure. Groups 1 and 2 served as controls. Drug treatment was initiated after pacemaker implantation and lasted 5 weeks. Animals were sacrificed and the hearts were studied with electrodes for a variety of electrophysiologic parameters.

Results: Eplerenone did not prevent development of ventricular dysfunction in RVP dogs. The eplerenone + RVP group had similar depression in left ventricular ejection fraction (LVEF) and increase in LV dimensions as the placebo + RVP group. Alterations in LV conduction, repolarization, and refractoriness were noted in the placebo + RVP group, but not in the placebo with no RVP group. Eplerenone prevented many of these pathologic changes from occurring. The eplerenone + RVP group had less inducibility of VA (40%) compared to the placebo + RVP group (82%). Even when VA was induced in the eplerenone + RVP group, a more aggressive induction protocol had to be used.

Conclusions: This animal model study indicates that selective aldosterone blocker therapy significantly attenuates negative electrical remodeling in the ventricles. As a result, the arrhythmogenic substrate for life-threatening VAs and sudden cardiac death is modified and the vulnerability to these arrhythmias is significantly decreased.

Reviewer’s Comments: I think this study sheds light on an important benefit of aldosterone antagonist agents. Although this study is conducted in an animal model, I think that it is important to share some of its findings. I left much of the basic science details out and chose the pertinent clinical pearls. Aldosterone antagonists are gaining a foothold in the treatment of heart failure patients, but more physicians need to familiarize themselves with the benefits and indications of these agents. (Reviewer-Khalid Almuti, MD).

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Keywords: Aldosterone-Antagonist, Eplerenone, Ventricular Tachyarrhythmias

Print Tag: Refer to original journal article
Can Osteoporosis Tx Help Patients Avoid Open Heart Surgery?

Osteoporosis Treatment and Progression of Aortic Stenosis.

Skolnick AH, Osranek M, et al:

Am J Cardiol 2009; 104 (July 1): 122-124

Osteoporosis treatment is strongly and independently associated with decreased progression of aortic stenosis.

**Objective:** To investigate the link between low bone mineral density and aortic stenosis (AS) progression, and a possible medical treatment to slow the progression of AS.

**Design/Methods:** Retrospective look at a small number of patients (n=55) at NYU with AS between 2002 and 2004. Eighteen of these patients were on 1 of 3 osteoporosis treatments available: bisphosphonates, calcitonin, or selective estrogen receptor modulators. The treatment group (OT+) was then compared to 37 patients with similar demographics without osteoporosis treatment (OT-). All patients had an index echocardiogram with a follow-up study at 1 year. The valve area of all patients was calculated using the continuity equation by an expert blinded to the treatment status and date of examination. Patients with other valvular diseases, renal insufficiency, hyperparathyroidism, and left ventricle dysfunction at baseline were excluded.

**Results:** Both groups at baseline had statistically similar measurements with an aortic valve area (AVA) of 1.29 cm² for the OT+ group, and 1.39 cm² for the OT- group. Both groups had a decrease in their AVA; however, progression of the OT+ group (0.10 ± 0.18 cm²/year) was significantly less than that in the OT- group (0.22 ± 0.22 cm²/year). In this multivariate study including age, gender, and statin therapy, only OT+ showed significant slowing of AS.

**Conclusions:** Osteoporosis medications may be associated with slowing the progression of AS.

**Reviewer's Comments:** This article is obviously limited by its small size and retrospective design; however, one cannot deny its pragmatic approach to a common cardiac issue that clinicians face every day. As of today, there are no approved medical treatments available for AS. Moreover, since the majority of AS patients are elderly, slowing down the progression of this disease even by a few years can potentially save a fragile patient an open heart surgery. While the results of this study are far from making this a standard of care, it does provide a novel approach to a clinical question. It will also be interesting to see the results of this medical therapy in a broader and larger patient population, such as patients with renal failure, bioprosthetic valves (mentioned by the authors), and even bicuspid aortic valves. The relatively low side-effect profile of these medications (perhaps with the exception of the estrogen receptor modulators) makes them an obvious possibility for medical treatment of AS. (Reviewer-Behnam Bozorgnia, MD).

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Keywords: Osteoporosis Treatment, Aortic Stenosis

Print Tag: Refer to original journal article
Regadenoson and adenosine perfusion nuclear studies result in similar quantitative levels of perfusion defects and extent of ischemia.

**Background:** Pharmacologic nuclear stress testing with adenosine has long been shown to have both diagnostic and prognostic utility in patients with suspected coronary artery disease. In order for regadenoson, a selective adenosine A2A receptor agonist to be useful clinically, it should show at least similar diagnostic and prognostic utility as adenosine.

**Objective:** To quantitatively compare perfusion and function between regadenoson and adenosine nuclear studies.

**Design/Methods:** In this sub-study analysis of the ADVANCE MPI 2 (Adenosine versus Regadenoson Comparative Evaluation for Myocardial Perfusion Imaging) trial, investigators quantitatively assessed perfusion and function results in 260 patients randomized to adenosine infusion and 495 patients randomized to regadenoson. Both these groups had had an unblinded adenosine study within the previous 4 weeks.

**Results:** The study quality in the serial adenosine-adenosine and adenosine-regadenoson groups was similar. Overall, 40% of patients in each group had a clearly abnormal perfusion study. The overall agreement between the adenosine-adenosine and adenosine-regadenoson studies was similar using visual interpretation of the scans (95.0% agreement between adenosine-adenosine vs 97.5% between adenosine-regadenoson scans; \( P = \text{NS} \)). There were no differences in quantitative assessment of perfusion defect size, ischemia severity, or gated SPECT variables, such as left ventricular ejection fraction and volumes between adenosine and regadenoson groups. Overall perfusion defect size in both groups was approximately 11% of the myocardium. Similarly, there were no differences in perfusion results in serial adenosine-regadenoson studies.

**Conclusions:** Regadenoson and adenosine perfusion nuclear studies result in similar quantitative levels of perfusion defects and extent of ischemia.

**Reviewer's Comments:** This sub-study of the ADVANCE MPI 2 study demonstrates that regadenoson induces similar perfusion defect size and extent of ischemia as adenosine, and thus the 2 agents are comparable when used clinically. Regadenoson is a selective A2A adenosine receptor agonist that causes coronary vasodilatation and increases coronary blood flow by >2.5 times normal. Adenosine acts on the same receptors, but it also acts on other receptors, such as adenosine A1, A2B, and A3 receptors, leading to side effects like heart block and bronchospasm. Regadenoson is attractive for clinical use due to its ease of administration (0.4 mg bolus vs 6-minute infusion for adenosine) and potential lack of significant side effects like heart block and bronchospasm. This study lends confidence to clinicians who have started using regadenoson in their practice. (Reviewer-Anoop C. Parameswaran, MD).

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Keywords: Single-Photon Tomography, Regadenoson, Adenosine

Print Tag: Refer to original journal article
Background: Radiation dosage remains a concern as cardiac CT angiography (CCTA) rapidly spreads as a means of noninvasively imaging the coronary arteries. Some single-center studies have shown reduced radiation dosage by using a lower tube current voltage.

Objective: To compare a 120 kV versus 100 kV tube voltage in a pre-defined subgroup from a large prospective study.

Design/Methods: The PROTECTION (Prospective Multicenter Study on Radiation Dose Estimates of Cardiac CT Angiography I) study was a multicenter survey study on radiation dose of CCTA in clinical practice. Overall, 82 patients in whom 100 kV tube voltage were applied and 239 patients in whom 120 kV were used were selected from this study. An image quality score, image noise, signal-noise ratio, contrast-noise ratio, and radiation dosage were calculated.

Results: Of 1965 patients evaluated in the PROTECTION I study, only 82 (4.2%) were scanned using 100 kV tube voltage. Baseline characteristics of both groups were similar, except for body weight and body mass indices being lower in the 100 kV group (72.0 kg vs 79.4 kg and 24.2 kg/m² vs 26.6 kg/m²). More than 95% of patients in both groups had a spiral scan acquisition mode. The CT dose index was 52.2 mGy vs 23.6 mGy in those scanned with 120 kV vs 100 kV. The dose length product was also significantly lower with 100 kV compared with 120 kV (376 vs 808 mGy x cm). The radiation dose decreased from a median of 14 mSv to 6 mSv when using 100 kV. Lowering of tube voltage increased image noise, but also improved signal intensity, signal-noise ratio, and contrast-noise ratio. The image quality scores were no different between the 2 groups.

Conclusions: Using 100 kV tube current significantly lowers radiation exposure without a significant effect on image quality.

Reviewer's Comments: Despite having the limitations of a nonrandomized study design, this is an important study. Radiation dose changes approximately with the square of the tube voltage. Thus, slight reductions in tube voltage will lead to significant reductions in radiation exposure. Despite increasing image noise, the diagnostic image quality score was not affected. In fact, by increasing the signal intensity, image-to-noise and contrast-to-noise ratio may lead to improved visualization of coronary arteries, though this was not evaluated in this study. Combining a reduced tube voltage with prospective ECG gating (as opposed to retrospective gating) can potentially lead to even lower radiation exposure (<3 mSv) and holds great potential. (Reviewer-Anoop C. Parameswaran, MD).

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Keywords: CT, Coronary Artery Disease, Tube Voltage

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