Background: Although cardiac CT angiography (CTA) is predominantly used to detect atherosclerotic coronary artery disease (CAD), many incidental but clinically significant cardiac abnormalities may be found.

Objective: To identify unsuspected cardiac lesions in a large cohort of patients who underwent CTA.

Participants/Methods: 4543 consecutive patients with mean age of 60 ± 13 years who were undergoing CTA for a clinical indication were studied. Scans were performed using a 64-slice scanner and a dual-source scanner. Retrospective gating was used. Only potential vascular abnormalities with clinical implications were included.

Results: 201 of 4543 patients (4.4%) had incidental nonatherosclerotic cardiac abnormalities identified. Of these abnormalities, 151 (75%) were previously known or suspected, and 25% (50) were new findings detected for the first time. Fifteen of these 50 patients had major interventions done because of this new diagnosis; 88% of the 50 patients had experienced some symptoms judged to be cardiac in nature. The largest group of incidental findings involved an anomalous coronary arterial origin (19 patients). The most common was the right coronary artery from the left coronary sinus. Eleven patients had ascending aortic aneurysms identified, 2 of whom had bicuspid aortic valves. Seven patients had hypertrophic cardiomyopathy, 4 patients had valvular heart disease (1 mitral stenosis and 3 bicuspid aortic valves), and 3 patients had congenital heart disease (1 noncompaction of the myocardium and 2 ventricular septal defects). Three patients had pulmonary embolism, 1 had left atrial myxoma, 1 had apical aneurysm, and 1 had cardiomyopathy. Of the 50 patients, 20 had prior echocardiograms that did not diagnose the abnormality. In 9 of 151 patients in whom the abnormality was previously known, CTA was able to provide further details in a clinically relevant fashion.

Conclusions: 1% of patients undergoing coronary CTA at a major institution had clinically relevant, previously unknown vascular findings not related to obstructive CAD. A significant proportion of these patients had implications for subsequent therapy. This underscores the need for comprehensive reading of coronary CTA with careful assessment of scans in order not to miss important abnormalities.

Reviewer's Comments: As the volume of CTA continues to grow, there can be a tendency to rapidly assess the coronary tree for obstructive CAD and thereby miss other potentially important findings. In this study, the authors found unsuspected abnormalities in 1% of the scans; 30% of these had important interventions performed as a direct result of these findings. Thorough interpretation of CTA scans is, therefore, important as previously undetected and clinically important findings may be uncovered on a routine CTA. (Reviewer-Anoop C. Parameswaran, MD).

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Keywords: CT Angiography, Coronary Artery Disease, Coronary Anomaly

Print Tag: Refer to original journal article
Optimal medical therapy is similar to medical therapy plus percutaneous coronary intervention in patients with CAD regardless of age.

**Background/Objective:** Whether disparities in treatment and outcomes exist in older patients with stable CAD is not well known. The aim of the study was to assess the achieved treatment targets and cardiovascular outcomes in patients aged <65 years versus ≥65 years among those enrolled in the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial.

**Methods:** This was a post-hoc analysis of the COURAGE trial that randomized 2287 patients with stable CAD to either percutaneous coronary intervention (PCI) plus optimal medical therapy or optimal medical therapy alone. Baseline characteristics, treatment targets, and outcomes after a median of 4.6 years of follow-up were compared among those aged <65 years versus ≥65 years.

**Results:** No baseline differences were found between treatment groups in either age category. Angiographic findings among those randomized to PCI were similar for both age groups. Among older patients (≥65 years), the death rate was almost double that of younger patients (12% vs 4% to 6%). The rate of death or MI was also higher among older patients (21% to 23% vs 16%). There were no differences in MI, stroke, or hospitalization for unstable angina between age groups. Despite a higher mortality and higher incidence of death or MI among older patients, the addition of PCI did not reduce this risk. The rates of death and MI were similar in older patients randomized to medical therapy versus medical therapy plus PCI. The percentage of patients free of angina in the medical-therapy arm and PCI-plus-medical-therapy arms were similar at 60 months of follow-up in both the older and younger age groups (70% to 80%). Achievement of targets for blood pressure, cholesterol, diet, and exercise did not differ among age or treatment groups.

**Reviewer’s Comments:** This study lends further proof that, regardless of age, optimal medical therapy should remain the initial treatment strategy for patients with stable CAD. Also reassuring is the lack of increased adverse events among those ≥65 years of age who underwent PCI. (Reviewer-Anoop C. Parameswaran, MD).

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**Keywords:** Percutaneous Coronary Intervention, Optimal Medical Therapy, CAD

**Print Tag:** Refer to original journal article
No significant difference has been found in long-term mortality between primary PCI and fibrinolytic therapy for STEMI in observational studies.

**Background:** Multiple randomized, controlled trials (RCT) have demonstrated the advantage of primary percutaneous coronary intervention (PPCI) over fibrinolytic therapy in ST-segment elevation myocardial infarction (STEMI) with reduced mortality, reinfarction, and stroke. The reproducibility of these outcomes in the real world experience has been questioned.

**Objective:** Outcomes of patients with STEMI in RCTs and observational studies comparing PPCI and fibrinolytic therapy were assessed to identify potential differences.

**Methods:** Bayesian hierarchical random-effect meta-analyses were performed for 23 RCTs including 8140 patients and 32 observational studies including 185,900 patients.

**Results:** Primary PCI was associated with a significant 34% reduction in short-term mortality, a 64% reduction in stroke, and a 65% reduction in reinfarction in RCTs versus 23%, 61%, and 42% reductions in the observational studies, respectively. All of these findings were statistically significant. Long-term mortality was significantly reduced by 24% and reinfarction by 51% in the RCTs, but there was a statistically nonsignificant trend in long-term mortality reduction and reinfarction in the observational studies.

**Conclusions:** Primary PCI compared to fibrinolytic therapy was associated with short-term reductions in mortality, reinfarction, and stroke in patients with STEMI in both the RCTs and observational studies. Long-term mortality and reinfarction were significantly less in the RCT PPCI group, but only statistically nonsignificant trends were found favoring the PPCI group in the observational studies.

**Reviewer's Comments:** There are clear benefits of PPCI in STEMI in RCTs. There are potential biases in RCTs; some of these trials excluded patients who were elderly or who had renal failure, cardiogenic shock, greater than Killip class II heart failure, and left bundle branch block, providing a potentially less ill population than in observational studies. These patients were also treated in selected institutions with highly experienced operators and processes to ensure acceptable door-to-balloon times. The authors showed a correlation between RCTs and observational studies relative to short-term outcomes. However, there is less impressive correlation in long-term outcomes. The RCTs demonstrated significant long-term benefits in mortality and reinfarction, while the observational studies showed only nonsignificant trends toward benefit. The findings could be due to biases described above. There were sicker patients in the PPCI group, with more anterior STEMI, more heart failure, and more cardiogenic shock in the observational studies. Similarly, the RCTs had a lower rate of in-hospital PCI after fibrinolysis than did the observational studies. Any or all of these potential confounding biases could affect outcomes. Primary PCI is still the treatment of choice for STEMI in institutions that have the process to accomplish target door-to-balloon times. The study alerts physicians to assess their programs and ensure that there are reasonable door-to-balloon times, appropriate patient selection, skilled operators, and processes to as closely match the RCTs outcomes as possible. (Reviewer-D. Lynn Morris, MD).

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Keywords: Primary Percutaneous Coronary Intervention, Fibrinolytic Therapy, ST-Segment Elevation Myocardial Infarction

Print Tag: Refer to original journal article
Does Metoprolol Improve QOL in Vasovagal Syncope?

Effect of Metoprolol on Quality of Life in the Prevention of Syncope Trial.
Sheldon RS, Amuah JE, et al:

J Cardiovasc Electrophysiol 2009; 20 (October): 1083-1088

Metoprolol does not improve the quality of life in patients with recurrent vasovagal syncope and a positive head-up tilt-table test.

**Background:** Vasovagal syncope is a common medical problem that is responsible for a substantial number of physician office visits and hospitalizations. In addition to education, pharmacologic therapy is frequently attempted with varying success. Beta-blockers, specifically metoprolol, are often used for this purpose with little data regarding the effect on quality of life (QOL). The Prevention of Syncope Trial (POST) was a double-blind, randomized, controlled trial comparing metoprolol to placebo in patients with vasovagal syncope.

**Objective:** To assess the effect of metoprolol on QOL in patients with recurrent vasovagal syncope.

**Methods:** This study was a prespecified subgroup analysis of the POST trial. Patients with recurrent syncope and a positive head-up tilt table test with or without isoproterenol infusion were randomized based on age (<42 or ≥42 years) to receive placebo or metoprolol 50 mg twice a day increased to 100 mg twice a day after 3 to 5 days if tolerated. Medications were continued for 1 year. Each patient underwent standardized questionnaires at baseline and at 6 and 12 months to measure extent of syncope, health status, and QOL.

**Results:** In total, 208 patients were randomized to the 2 arms. The mean age was 42 years, and 64% were female. Enrolled patients had a median of 9 syncopal episodes over a median of 11 years. Triggers for syncope and comorbidities were balanced between the 2 groups. The main study has previously reported no significant treatment effect. Approximately 40% of patients withdrew from the study by 12 months, most commonly because of fatigue, presyncope, and insomnia. Metoprolol demonstrated no benefit in QOL. The age group (ie, <42 or ≥42 years old) had no effect on response to metoprolol.

**Conclusions:** Metoprolol appears to have no appreciable benefit on QOL in patients with vasovagal syncope.

**Reviewer’s Comments:** Vasovagal syncope is a common problem faced by cardiologists. In cases where education and lifestyle modifications prove unsuccessful, empiric initiation of a variety of pharmacologic agents is often attempted. The POST trial in this subgroup analysis indicate that metoprolol is not an effective treatment in an unselected group of patients with vasovagal syncope and positive head-up tilt-table testing. It is possible that a noncardioselective beta-blocker may have been more effective. Unfortunately for us and our patients, no silver bullet for vasovagal syncope seems to exist. (Reviewer-Sumeet K. Mainigi, MD).

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Keywords: Syncope, Vasovagal, Neurocardiogenic

Print Tag: Refer to original journal article
Do not reflexively withhold chronic beta-blocker therapy in all patients with acute decompensated heart failure.

**Background:** The issue of what to do with maintenance beta-blocker (BB) agents during acute decompensated heart failure (ADHF) has been a matter of debate for some time. Many physicians withhold or decrease the dose of BB due to concerns about its negative inotropic effects. Some evidence suggests that withholding BB may be harmful to patients. The B-CONVINCED (Beta-Blocker CONtinuation Vs. INterruption in Patients With Congestive Heart Failure Hospitalized for a Decompensation Episode) trial addresses this issue.

**Objective:** To investigate the effect of continuing versus withholding maintenance BB in patients with ADHF.

**Methods/Participants:** Patients with systolic heart failure (HF) and LVEF <40% presenting with ADHF were included. They must have been on stable BB therapy for at least 1 month previously. A total of 147 patients were randomized to either continued BB therapy at a chronic dose or discontinuation of BB for at least 3 days. Subjective and objective measures of HF status were collected at 3 and 8 days, including treating physician and patient surveys. The primary end point was the proportion of patients who improved (general well-being and dyspnea) at 3 days. Patients with heart block or STEMI were excluded.

**Results:** The 2 groups were similar in baseline demographics and in the HF presentation and level of BNP. BB agents included bisoprolol (70%), carvedilol, and atenolol. Few patients who required dobutamine therapy had their BB withheld. During follow-up, the clinical features of HF improved similarly in both groups. Blood pressure changes followed similar trajectories in both groups. Heart rate decreased more significantly in the BB-maintained group. At 3 days, there were no significant differences in the primary end point between the 2 groups from the treating physician's standpoint, indicating no benefit to withholding BB. From a patient’s standpoint, maintaining BB therapy was associated with a statistically insignificant improved outcome (88%) versus withholding therapy (82%). Similar findings were recorded at 8 days after enrollment. Changes in BNP were similar between groups. Of importance, the proportion of patients on BB at 3 months poststudy was much higher in the BB-maintained group (90%) versus the BB-stopped group (76%; \( P = 0.04 \)).

**Conclusions:** This study demonstrates that there is no need to withhold BB therapy in patients presenting with ADHF as clinical improvement was similar between both groups. The only exception is when dobutamine therapy is needed, in which case BB should be stopped. Stopping BB during hospitalization may lead to patients being discharged without BB (possibly due to forgetfulness), which deprives patients of the well-documented benefit of chronic BB therapy for systolic HF.

**Reviewer's Comments:** This trial supports earlier retrospective studies indicating that the practice of routinely stopping chronic BB therapy in ADHF patients is unnecessary. Some argue that this practice may even be harmful to certain patients. BB therapy should be stopped only if there is a compelling indication (ie, bronchospasm, marked hypotension, or initiation of dobutamine). (Reviewer-Khalid Almuti, MD).

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Keywords: Maintenance Beta-Blockers, Decompensated Heart Failure

Print Tag: Refer to original journal article
Using a validated clinical risk prediction model may identify patients at such high risk of mortality that ICD therapy is unlikely to be of benefit.

**Background:** Current guidelines make a Class I recommendation for the prophylactic implantation of a defibrillator (ICD) in patients with NYHA class 2 to 3 symptoms and an ejection fraction (EF) ≤35%. However, only 20% to 25% of primary prevention ICD patients receive appropriate shocks within 5 years of implantation.

**Methods:** The Seattle Heart Failure Model (SHFM) is a multivariate risk model that predicts all-cause and cause-specific mortality in heart failure (HF) patients. It has been extensively validated. A modification of the SHFM was applied to data from the SCD-HeFT randomized trial (one of the seminal studies leading to the recommendation for prophylactic ICD placement).

**Results:** As a percentage of total mortality, the proportion of sudden cardiac deaths (SCD) in the placebo group decreased with increasing SHFM-predicted mortality. In the overall trial, ICD use decreased the relative risk of SCD by 62% ($P<0.0001$). However, the benefit was greater in those with low-risk SHFM scores than with high scores; this was true despite similar rates of appropriate shocks across quintiles of SHFM score. When absolute mortality was evaluated, no benefit with ICD therapy was seen in the highest quintile. Numbers needed to treat for 4 years to save 1 life varied from 1.5 in the lowest quintile to 7 in the fourth quintile to no benefit in the highest risk quintile.

**Conclusions:** Risk stratification via application of a model derived from routine clinical variables can accurately identify patients with systolic HF; it can also predict the benefit (or lack) of primary-prevention ICD therapy.

**Reviewer’s Comments:** This is an important study in the effort to tease out systolic HF subjects who are likely to benefit from prophylactic ICD therapy. It is known that patients with lower total mortality risk die primarily from SCD, while those with higher overall mortality risk have an increased risk of dying from pump failure. It is also well known that many patients receiving an ICD will never use it. The authors point out that previous efforts to refine selection have focused on test-based measures such as microvolt T-wave alternans. Application of a validated clinical risk model has obvious advantages, as it focuses on routinely collected information such as age, gender, ischemia, blood pressure, EF, medications used, and serum sodium. Many patients do not want an ICD. Many times physicians are reluctant to place them, and the devices are associated with significant risks and cost. If this approach to gauging device benefit can be confirmed in future studies, it will greatly refine our therapeutic accuracy in this difficult-to-manage patient population. (Reviewer-Gregg S. Pressman, MD).

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Keywords: Systolic Heart Failure, Sudden Cardiac Death, Prophylactic ICD

Print Tag: Refer to original journal article
Compared to stable patients, patients with acute coronary syndrome treated with either BMS or DES are at increased risk for both early and late stent thrombosis.

**Background:** Drug-eluting stents (DES) have consistently reduced the need for repeat revascularizations compared to bare-metal stents (BMS). Given that endothelialization of the stent is delayed in DES, there has been concern regarding the risk of late and very late stent thrombosis. Mechanical risk factors for late stent thrombosis include late incomplete stent apposition that may occur after thrombus resolution in the setting of acute coronary syndrome (ACS). One meta-analysis of trials that randomized ST-segment elevation myocardial infarction (STEMI) patients to DES versus BMS showed equivalent risk of stent thrombosis up to 12 months. Whether there is increased risk of stent thrombosis with the use of DES in ACS in the “real world” with longer follow-up is not known.

**Methods:** This was a registry study from the Thoraxcenter in the Netherlands. All patients who were treated with a single type of stent for a documented indication between January 2000 and December 2005 were included. The registry consisted of 3 sequential groups as the default stent changed over time: BMS until April 2002, then sirolimus-eluting stent (SES) until February 2003, then paclitaxel-eluting stent (PES). The primary end point was definite stent thrombosis: angiographically documented stent thrombosis with acute symptoms. Follow-up data were obtained from questionnaires and from municipal civil registries with regard to death.

**Results:** Of 5816 patients treated with DES or BMS, 3546 were for ACS. Follow-up data were available for 98% patients for a median of 1394 days. DES patients were treated with clopidogrel for a longer duration (6 vs 2 months for BMS). Compared to stable patients stented during the same time period, patients with ACS were overall at a higher risk for stent thrombosis for all time points regardless of the type of stent used. There was a nonsignificant trend toward an increase in very late stent thrombosis with DES in ACS. As expected, there was an increase in mortality associated with stent thrombosis.

**Reviewer’s Comments:** This study confirms that ACS patients, presenting with either non-STEMI or STEMI, are at increased risk for stent thrombosis, regardless of the type of stent used. Interestingly, no significant differences were seen between STEMI and NSTEMI patients. The duration of thienopyridine treatment post-DES was shorter than would be recommended today, although within the first year post-stent, this did not affect the relative risk of stent thrombosis compared to BMS. The trend toward an increase in very late stent thrombosis with DES in ACS may be attributable to mechanical factors, although small differences in an observational design make it difficult to draw definitive conclusions. These findings indicate the importance of meticulous interventional practice in ACS to avoid mechanical factors such as stent underexpansion and edge dissections that might eventually lead to stent thrombosis. (Reviewer-Parul B. Patel, MD).

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Keywords: Acute Coronary Syndrome, Stent, Thrombosis

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Severe functional TR can occur years after left-sided valve surgery.

**Background:** Clinically significant tricuspid regurgitation (TR) is increasingly recognized as a late complication of previous left-sided valve surgery (especially of the mitral valve). While it adversely impacts prognosis, high surgical morbidity/mortality have been reported.

**Participants/Methods:** 61 consecutive patients with severe TR referred for surgical correction were studied with Doppler echocardiography and followed clinically. Fifty (82%) were in atrial fibrillation and 51 (84%) had functional TR (ie, due to annular dilation and/or papillary muscle displacement). Fifty-seven (93%) had previous left-sided valve surgery, and 8 underwent repair, while 53 had replacement (30 tissue valves, 23 mechanical valves). Median follow-up was 32 months (range, 12 to 70 months).

**Results:** Operative mortality was 10% (6 patients); 3 others died during follow-up (2 of heart failure, 1 with hemorrhagic stroke). At the end of follow-up, 75% were event free. These subjects had more favorable NYHA class, lower creatinine, and higher albumin, platelet and hemoglobin levels. On echocardiography, event-free survivors had lower preoperative right ventricular (RV) end-systolic area and higher RV fractional area change (EF surrogate). At 6 months follow-up, 33 (61%) of 54 survivors showed improved functional capacity. Multivariate analysis showed hemoglobin and RV end-systolic area (on apical 4 chamber) to be the most important predictors of event-free survival. Two-year event-free survival was 90% with hemoglobin >11.3 versus 44% otherwise, and 91% if RV end-systolic area was <20 cm² versus 57% otherwise. Though preoperative NYHA class was not independently predictive, 2-year event-free survival was 90% predictive for class II vs 68% for class III/IV.

**Conclusions:** Severe TR has a significant operative mortality. However, reasonable event-free survival and improvement in functional capacity can be expected in survivors. RV end-systolic area <20 cm² (corresponding to ≤ moderate dilation), NYHA class II and hemoglobin >11 predicted lower operative mortality and improved survival in this study.

**Reviewer’s Comments:** TR developing late after left-sided valve surgery is becoming recognized as a growing problem. It can occur years later, even when only mild TR was present at the time of surgery. When present, severe TR substantially worsens survival. This has lead to guideline recommendations for tricuspid annuloplasty at the time of left-sided valve surgery if the tricuspid annulus is dilated (>35 to 40 mm between the septal and lateral leaflet attachments on the apical 4-chamber view). Prevention of future TR is important since tricuspid valve surgery has high morbidity and mortality as demonstrated in this study. Another under-recognized cause of TR is iatrogenic following placement of a pacemaker or defibrillator leads. Such leads can entangle valve leaflets and/or chordae and perforate leaflets or push them aside, interfering with normal coaptation. On occasion, the resultant TR can be severe. (Reviewer-Gregg S. Pressman, MD.)

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Keywords: Functional Tricuspid Regurgitation, Surgical Repair, Prior Left-Sided Valve Surgery

Print Tag: Refer to original journal article
Anger, Hostility Associated With CHD


Chida Y, Steptoe A:

J Am Coll Cardiol 2009; 53 (March 17): 936-946

Anger and hostility increase the risk of CHD and worsen its prognosis.

**Background:** Epidemiological data suggest psychosocial stressors influence the development and prognosis of coronary heart disease (CHD). Depression, which has been extensively studied, can be considered a risk factor for CHD that is comparable to traditional risk factors like hypertension. Psychosocial stressors promote high-risk behaviors such as poor diet, decreased physical activity, smoking, and decreased medicine compliance. Some data suggest that psychosocial stressors negatively affect biological pathways (including autonomic nervous system dysregulation) and increases in inflammatory and coagulation factors. Several reviews examining the association of anger and hostility with CHD have produced disparate findings, likely due to a lack of distinction between prospective, cross-sectional studies versus retrospective cohort studies.

**Design/Definitions:** In this meta-analysis of prospective cohort studies exploring the association of anger and hostility with CHD, hostility is defined as a negative attitude or cognitive trait directed towards others. Anger is an emotional state consisting of feelings that vary in intensity from mild irritation to rage and can be manifested with verbal or physical behavior ranging from yelling to physical assault.

**Methods:** Criteria for inclusion of studies included full-length, English language publications in peer reviewed journals, prospective cohort studies, and investigations of the longitudinal association between anger and hostility in the development/prognosis of CHD.

**Results:** There were 25 studies investigating CHD outcomes in healthy populations and 19 studies in subjects with existing CHD; 71,606 healthy individuals and 8120 CHD subjects were included. Anger and hostility were associated with increased CHD events in a healthy population (HR, 1.19), and with poor prognosis in the CHD population (HR, 1.24). Subgroup analysis showed longer follow-up studies exhibited higher HRs. Interestingly, studies that differentiated between sexes showed a more harmful association with anger and hostility in men. Analysis focusing only on CHD mortality showed that anger and hostility were associated with increased mortality in CHD subjects studies (HR, 1.18), but not in healthy population studies.

**Conclusions:** This study suggests that anger and hostility are associated with CHD outcomes in healthy and CHD populations. The authors propose that beyond conventional pharmacological interventions, psychological management focusing on anger and hostility may help in the prevention and treatment of CHD.

**Reviewer's Comments:** This is the first quantitative systematic review to show that anger and hostility are significantly associated not only with increased CHD events in healthy populations, but also with a poor prognosis in patients with existing CHD. Although the risk incurred by anger and hostility of 20% is relatively small, it is comparable to traditional risk factors. Studies reviewed were observational and, therefore, cannot definitively establish causality. These results suggest that successful prevention and treatment of CHD might involve a multidisciplinary approach, including not only conventional physical and pharmacological therapies, but also psychological management focusing on anger and hostility. (Reviewer-Vincent M. Figueredo, MD).

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Keywords: Anger, Hostility, Coronary Heart Disease

Print Tag: Refer to original journal article
Patients treated with omeprazole have a diminished platelet response to clopidogrel compared to those treated with pantoprazole.

**Background:** Clopidogrel is a potent antiplatelet agent often used post-stenting to prevent peri-procedural ischemic events. However, a wide variability in platelet inhibition has been demonstrated among patients treated with clopidogrel, and a reduced response has been associated with increased ischemic events. Given that clopidogrel is a prodrug requiring activation by the hepatic CYP450 enzyme, there has been concern over concomitant use of drugs that might affect this process. Omeprazole is one such drug that has been shown to reduce the efficacy of clopidogrel by platelet reactivity tests. Other, newer proton-pump inhibitors (PPIs), such as pantoprazole and esomeprazole, have not had this effect.

**Objective:** To compare the relative effects of omeprazole and pantoprazole on platelet reactivity tests among patients with non–ST-segment elevation acute coronary syndrome (NSTE ACS) who underwent stenting and were treated with a clopidogrel loading dose followed by a high maintenance dose.

**Methods:** Patients were loaded with clopidogrel 600 mg and aspirin 250 mg at least 12 hours prior to stenting. Baseline platelet parameters were obtained after loading. At discharge, patients were prescribed aspirin 75 mg and clopidogrel 150 mg daily, and were randomized to either omeprazole 20 mg or pantoprazole 20 mg daily. Platelet testing was repeated at 1 month. The primary end point was clopidogrel response at 1 month.

**Results:** 104 consecutive patients were randomized to either omeprazole or pantoprazole. Baseline platelet reactivity after a clopidogrel loading dose was similar between the 2 groups. At 1 month, the platelet response to clopidogrel was significantly greater in the pantoprazole group. There were also more clopidogrel nonresponders in the omeprazole group than in the pantoprazole group.

**Reviewer's Comments:** Proton-pump inhibitors are metabolized by the 2C19 isoform of CYP450. A loss of function allele of this enzyme has been associated with a diminished response to clopidogrel and increased ischemic events in patients treated with clopidogrel. This study demonstrates that the degree to which different PPIs are metabolized by CYP2C19 may vary, and therefore, different PPIs may impact the response to clopidogrel differently. Although clinical events were not included in this small study, the results suggest that pantoprazole is a better choice for clopidogrel-treated patients. Of note, COGENT, a much larger study comparing omeprazole to placebo in clopidogrel-treated patients found no difference in terms of ischemic end points at a mean follow-up of 133 days. There was, however, a reduction in gastrointestinal events with the PPI. I would conclude that treatment with a PPI should not be withheld from clopidogrel-treated patients who need it, and that perhaps pantoprazole might be the better choice. (Reviewer-Parul B. Patel, MD).

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**Keywords:** Clopidogrel Response, Proton Pump Inhibitor, Omeprazole, Pantoprazole

**Print Tag:** Refer to original journal article
Banning Smoking in Public Places Saves Lives

Cardiovascular Effect of Bans on Smoking in Public Places: A Systematic Review and Meta-Analysis.

Meyers DG, Neuberger JS, He J:

J Am Coll Cardiol 2009; 54 (September 29): 1249-1255

A ban on smoking in public places in the United States could prevent an estimated 156,000 new cases of acute myocardial infarction annually.

**Background:** Second-hand smoke (SHS) has deleterious effects on the cardiovascular health of nonsmokers, including an increase of 30% in the risk of acute myocardial infarction (AMI). Bans on smoking in public places have been implemented in many localities worldwide, with some reports of salutary effects on cardiovascular health.

**Design/Objective:** This meta-analysis was performed to estimate the overall effect of banning public smoking on the risk for AMI in the population.

**Methods:** A systematic review of the literature for peer-reviewed articles dealing with the subject (AMI, smoking bans) yielded 11 studies concentrating on 10 different geographic areas in North America and Europe. Each study compared the risk of AMI before and after the ban. Data were abstracted by 2 different researchers, and statistical analysis was performed with the aid of specialized statistical software.

**Results:** The review yielded results from 5 U.S., 1 Canadian, and 4 European localities ranging in population from 30,000 to 19 million people. The meta-analysis showed that the incidence rate ratio (IRR) for AMI, comparing periods of the time before and after the ban, was 0.83 (95% CI: 0.75 to 0.92). This implied a 17% risk reduction in AMI as a result of the smoking bans. Further statistical analysis suggested that the findings were not likely due to chance. Of note, one of the localities that banned smoking in public places had a beneficial effect on the risk of AMI that disappeared when the smoking ban was reversed by the judicial system.

**Conclusions:** This meta-analysis demonstrates that a ban on smoking in public places has significant beneficial effects on the incidence of AMI in the exposed population. The authors estimate that a general ban on smoking in public places in the United States may prevent an estimated 156,000 new cases of AMI annually!

**Reviewer's Comments:** These are interesting data that should give more impetus to efforts to restrict sources of SHS. The cost savings to the health care system from preventing all of these cases of AMI would be tremendous. This is without even considering other cardiovascular and general health benefits (ie, cancer) that would be expected from reducing SHS exposure. (Reviewer-Khalid Almuti, MD).

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Keywords: Public Smoking, Bans, Second-Hand Smoke

Print Tag: Refer to original journal article
Regadenoson is a useful, practical, and safe agent for MPI and may replace adenosine.

Background: Stress myocardial perfusion imaging (MPI) is widely used in the detection, assessment, and treatment of coronary artery disease (CAD). Half of the tests are now performed with vasodilators, such as adenosine and dipyridamole, rather than exercise. Regadenoson is a new agent that is a selective $A_{2A}$ agonist. Adenosine activates 4 receptor subtypes ($A_1$, $A_2$, $A_{2B}$ and $A_3$). $A_{2A}$ and $A_{2B}$ vasodilate coronary and peripheral arterial beds increasing myocardial blood flow and sympathoexcitation. $A_1$ receptors mediate negative chronotropic, dromotropic, inotropic, and anti–beta-adrenergic effects. Stimulation of $A_3$ and $A_{2B}$ causes bronchoconstriction. Regadenoson is a potent and selective vasodilator with a rapid onset of action when given as a fixed-dose bolus. It has a low affinity for the $A_{2A}$ adenosine receptor allowing maximal vasodilatation and rapid termination of action.

Objective: To describe regadenoson for MPI and compare it to adenosine.

Results: The hemodynamic effects of regadenoson include a decrease in mean arterial blood pressure in clinical trials. The heart rate increased with regadenoson and stayed higher longer than with adenosine. Regadenoson increases serum norepinephrine and epinephrine suggesting direct sympathoexcitation. Adenosine increases renal vascular resistance and renal vasoconstriction, but regadenoson does not. Two identical randomized, double-blinded, placebo-controlled trials showed excellent agreement between stress image interpretation between adenosine and regadenoson. The side-effect profile was good, with no incidences of high-degree atrioventricular (AV) block with regadenoson (patients with AV block were excluded at the start of the trial.) There were no deaths, life-threatening arrhythmias, or QT prolongation. Regadenoson was preferred because of less flushing, chest pain, and dyspnea. Adenosine might cause bronchospasm in patients with asthma or patients on bronchodilators or steroids and is usually avoided. A randomized, double-blind, placebo-controlled, crossover study of regadenoson was done in patients with proven mild or moderate asthma. The mean forced expiratory volume at 1 second (FEV$_1$) was not different in the regadenoson-treated patients compared to placebo-treated patients; bronchospasm occurred in 4% of both groups. There was no desaturation. There was more dyspnea with regadenoson than placebo, but not associated with a decrease in FEV$_1$. A similar trial with chronic obstructive pulmonary disease patients showed similar results. A larger study needs to be done on patients who are wheezing or are on bronchodilators. Regadenoson is becoming very popular, but adenosine will soon be available in the generic form.

Conclusions: Regadenoson has appealing features since it is easy to administer (bolus, not weight adjusted), has a fast onset, and has a short duration of action. It has comparable efficacy to adenosine, but with fewer side effects. Unlike adenosine, it can be used in patients with mild-to-moderate reactive airway disease and obstructive lung disease.

Reviewer's Comments: Regadenoson is an important addition to stress testing because of its side-effect profile allowing use in patients who could not be tested with adenosine. (Reviewer-Marjorie Stanek, MD).

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Keywords: Regadenoson, Stress Testing

Print Tag: Refer to original journal article
LVOT Gradient Varies Significantly in Hypertrophic Cardiomyopathy

Left Ventricular Outflow Tract Gradient Variability in Hypertrophic Cardiomyopathy.

Geske JB, Sorajja P, et al:
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LVOT gradient varies significantly in hypertrophic cardiomyopathy, which has important therapeutic value.

Background: Hypertrophic cardiomyopathy (HCM) is characterized by disproportionate hypertrophy of myocardium. Left ventricular outflow tract (LVOT) obstruction is usually present, and it is a dynamic phenomenon, dependent on the left ventricular load and contractility. However, the significant variations in the LVOT gradient, even on a day-to-day basis, may not be adequately assessed and taken into consideration when deciding on the best therapeutic options, including surgical, in symptomatic patients.

Objective: To test the hypothesis that LVOT gradient variability in HCM may have an impact on clinical decision making.

Participants/Methods: Included were 100 HCM patients who underwent 2-dimensional and Doppler transthoracic echocardiography (2-D echo) and cardiac catheterization with transseptal measurement of left-sided pressures. Transseptal catheterization was performed to avoid catheter entrapment. In the 100 patients, cardiac catheterization was performed for septal alcoholic ablation in 60 patients and for further classifying the LVOT gradient in the other 40 patients. Studies were all performed within 48 hours of each other.

Results: The correlation of LVOT gradients from both methods (2-D echo and catheterization) performed at different times, but within 48 hours, had a wide scatter. The 95% confidence limits of agreement were ± 84 mm Hg. Therefore, for classifying patients as having severe LVOT obstruction on the basis of either method (<30 vs ≥30 mm Hg), there were discrepant results in 21% of patients. Fifteen studies were performed with simultaneous measurement of LVOT gradient by both 2-D echo and catheterization, to confirm the accuracy of Doppler measurements. They revealed a very strong correlation (r = 0.98; P <0.0001) with 95% confidence limits of agreement ± 12 mm Hg.

Conclusions: There is significant and marked variability in LVOT gradients in patients with HCM. This variability needs to be adequately assessed before the most beneficial therapeutic option is advocated for the symptomatic patient.

Reviewer’s Comments: The estimation and characterization of the LVOT gradient is paramount when managing patients with HCM. LVOT obstruction is associated with an increase in mortality and morbidity. Therefore, management involves reducing or eliminating this gradient in patients with HCM. When medical therapy is inadequate in the symptomatic patient, surgical options, such as alcohol ablation or myomectomy, are often performed. A LVOT gradient >30 mm Hg is defined as severe obstruction. However, as this paper illustrates, LVOT gradients in HCM are dynamic, depending on contactility and loading conditions, which are affected by volume status, exercise, autonomic tone, diurnal variations, medical therapy, and patient positioning. Therefore, multiple measurements may ideally be required before actual severity can be assessed and optimal management can be offered. (Reviewer-Suraj Maraj, MD).

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Keywords: Left Ventricular Outflow Tract Gradient, Hypertrophic Cardiomyopathy, Variability, Management

Print Tag: Refer to original journal article
Effects of Thyroid Hormone Levels on CAD

Thyroid Hormone and Coronary Artery Disease: From Clinical Correlations to Prognostic Implications.

Coceani M, Iervasi G, et al:
Clin Cardiol 2009; 32 (July): 380-385

Active free triiodothyronine levels are inversely correlated to the presence of coronary artery disease.

**Background:** Hypothyroidism is a known cause of accelerated coronary artery disease (CAD). Also, low triiodothyronine (T3) syndrome, defined as reduced serum levels of both total and free T3 (fT3) with normal thyroid stimulating hormone and free T4 levels, is a strong prognostic factor in chronic, systolic heart failure. However, little is known about the fluctuations of fT3 within the physiological range and its possible relation to CAD.

**Objective:** To test the hypothesis that the occurrence of CAD, the long-term prognosis, and mortality in patients without a history of either primary thyroid disease, myocardial infarction (MI), or chronic heart failure (CHF) is related to serum levels of biologically active fT3 and low T3 syndrome.

**Participants/Methods:** 1047 clinically and biochemically euthyroid patients (median age, 65.6 years) underwent coronary angiography for suspected CAD. CAD was defined as a >50% stenosis in at least 1 major vessel or principal side branch. Thyroid hormones were measured prior to coronary angiography and patients were not on medications known to affect thyroid hormone sampling.

**Results:** Lower fT3 levels predicted both single-vessel ($P=0.012$) and multivessel ($P=0.009$) CAD, but, the difference in fT3 levels between single and multivessel disease was not statistically significant. Multivariate logistic regression analysis revealed fT3 was associated with CAD (hazard ratio, 0.48; 95% CI, 0.34 to 0.68; $P<0.001$). At a mean follow-up of 31 months, the survival rate was 95%, and total mortality ($P=0.009$) and cardiac mortality ($P=0.004$) was increased in patients with low T3 syndrome. This association between low T3 syndrome and survival was maintained even after further multivariate analysis (total mortality, $P=0.034$; cardiac mortality, $P=0.025$).

**Conclusions:** fT3 levels are inversely correlated to the presence of CAD. Also, after adjusting for traditional coronary risk factors, low T3 syndrome was still associated with an adverse prognosis and increased mortality.

**Reviewer's Comments:** Both overt hypothyroidism and subclinical hypothyroidism are established risk factors for CAD. However, this study illustrates that in the absence of primary thyroid disease or known clinical heart disease, lower fT3 levels are associated with CAD. This occurrence was seen both in the lower physiological values of fT3 as well as in low T3 syndrome. Also, low T3 syndrome was associated with a poorer prognosis on total and cardiac survival. Hypothyroidism leads to endothelial dysfunction, impaired fibrinolysis, hypercoagulability, and hyperhomocysteinemia. It is therefore possible that low fT3 and low T3 syndrome exert their negative cardiovascular effects due to similar mechanisms. (Reviewer-Suraj Maraj, MD).

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Keywords: Free Triiodothyronine, Coronary Artery Disease, Mortality, Prognosis

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Use of ultrasound contrast agents is safe in patients undergoing stress echocardiography.

**Background/Objective:** The safety of ultrasound contrast agents have been in question in recent years, which has led to revised recommendations for its use. The aim of this study was to assess the safety of ultrasound contrast agents in patients undergoing stress echocardiography (echo).

**Methods:** Mayo Clinic researchers retrospectively analyzed 29,759 patients who had stress echo done between 2003 and 2007. Those undergoing contrast echo using either Optison or Definity were compared with a noncontrast group. The primary outcome was death and myocardial infarction (MI) within 72 hours and after 30 days of stress echo. A secondary long-term outcome of death or MI up to 4.5 years was also assessed.

**Results:** Among the 29,759 patients, approximately 50% underwent contrast studies; 60.4% of patients in the contrast group underwent dobutamine stress echo, and 60.9% of patients in the noncontrast group underwent exercise stress echo. The average age was approximately 62 years in the noncontrast group and 65 years in the contrast group ($P <0.001$). Patients in the contrast group also had significantly greater cardiac risk factors than the noncontrast group. Despite this, the contrast group had similar rates of death and MI within 72 hours and in 30 days compared to the noncontrast group. The annualized event rate for MI or death in the dobutamine echo group who received contrast versus those who did not was similar (9.6% vs 10.9%). Among those who exercised, the annualized event rates for contrast versus noncontrast echo were lower, but not significantly (2.2% vs 1.9%). The proportion of patients with ventricular or supraventricular arrhythmias was also similar between the contrast and noncontrast groups.

**Conclusions:** Contrast agents did not increase the immediate or long-term adverse event rates when used in patients undergoing stress echo.

**Reviewer's Comments:** Due to post-marketing reports of 4 deaths within 30 minutes of contrast administration, the Food and Drug Administration (FDA) has issued strict recommendations for contrast use. These have recently been relaxed, but the black box warning still requires monitoring of patients with pulmonary hypertension and serious cardiopulmonary syndromes for 30 minutes after contrast injection. This study adds to the large body of evidence confirming the safety of contrast agents in real world clinical settings. Only 1 death occurred in the contrast group within 72 hours, but this was due to postoperative complications after repair of a mycotic aortic aneurysm. Given the tremendous clinical utility of contrast echo and given the proven safety of these agents in numerous studies, it may be time for the FDA to lift the black-box warning. (Reviewer-Anoop C. Parameswaran, MD).

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Keywords: Contrast Agent, Safety, Optison, Definity

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Cytochrome P450 converts clopidogrel to its active metabolite; smoking induces the P450 system.

**Background/Objective:** Cytochrome P450 converts clopidogrel to its active metabolite. Smoking induces the P450 system. The authors of this study investigate the effects of cigarette smoking on clopidogrel efficacy in ST elevation myocardial infarction (STEMI) population.

**Design:** Sub-group analysis of the large randomized Clopidogrel as Adjunctive Reperfusion Therapy-Thrombolysis In Myocardial Infarction 28 (CLARITY-TIMI 28) study.

**Participants/Methods:** 3,491 patients with STEMI were treated with fibrinolytic therapy, aspirin, and heparin and were randomized to a 300-mg loading dose of clopidogrel followed by 75 mg daily or placebo. All patients underwent coronary angiography 2 to 8 days after initiation of therapy. The primary efficacy end point of this study was Thrombolysis In Myocardial Infarction (TIMI) flow grade 0 or 1, recurrent myocardial infarction MI, or death before the angiography. The clinical end point was death, MI, or urgent revascularization within 30 days. Smoking status was available for 3,429 of this population; 1,732 were nonsmokers, 206 smoked 1 to 9 cigarettes/day, 354 smoked 10 to 19 cigarettes/day, and 715 smoked 20 to 29 cigarettes/day, and 422 smoked ≥30 cigarettes/day.

**Results:** Clopidogrel showed significant angiographic benefit for the entire trial cohort (reduced odds by 36%). However, among those who smoked one-half pack/day or more, the addition of clopidogrel resulted in a magnified benefit (20.5% to 11.7%) as compared to the nonsmokers or those who smoked <9 cigarettes/day, which showed more modest angiographic benefit (22.3% to 17.7%). More importantly, the 30-day clinical end point odds were also reduced by 20% in the heavy smoker group as compared to the nonsmoker group, which showed no benefit at all associated with the addition of clopidogrel.

**Conclusions:** Smoking positively modifies the beneficial effects of clopidogrel.

**Reviewer's Comments:** This study is academically interesting, and it points out the complexity of clopidogrel and the CYP450 system. The authors demonstrated the benefit of clopidogrel in the smoking population, but the conclusion of this study can be easily misinterpreted. Concluding that smoking is beneficial in the post MI population is rather simplistic. The benefit observed in this study is perhaps from the higher active metabolite of clopidogrel and increased antiplatelet activity due to induction of the P450 system in the smoking population. According to these data, one can conclude that higher doses of clopidogrel can have more benefit in the post-MI population treated with thrombolytics. It also brings up the question whether clopidogrel is under dosed. It will be interesting to follow the smoking population >30 days and compare the outcomes with the nonsmoking group. The detrimental effects of smoking may outweigh the induction of the P450 system. (Reviewer-Behnam Bozorgnia, MD).

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Keywords: Cigarette Smoking, Interaction, Clopidogrel, Clinical Benefit.
Those with larger areas of viable myocardium as determined by PET imaging derive greater benefit from revascularization.

**Background/Objective:** Patients with ischemic myocardial dysfunction may benefit from revascularization, but have a high operative mortality. Observational studies have shown that revascularization in the presence of viable myocardium improves outcomes. A recent randomized, controlled trial, the PARR-2 (positron emission tomography [PET] and Recovery Following Revascularization-2 (PARR-2) showed a trend toward improved outcomes in those whose revascularization was guided by PET results. 

**Design:** Post hoc analysis of the PARR-2 trial that sought to assess whether PET parameters could identify those who may benefit from revascularization.

**Methods:** Patients >18 years of age, with left ventricular ejection fraction <35% presumed to be due to coronary artery disease, who where considered for revascularization, transplant, or heart failure workup and in whom PET viability imaging was though to be useful in decision making by the treating physician were included in the initial PARR-2 study. Those randomized to the PET arm were included in this post hoc analysis. The group who underwent revascularization based on PET data was compared to those who underwent medical management.

**Results:** There were 182 patients in the PET arm, with an average age of 63 ± 10 years, 85% were male, and the mean ejection fraction was 26% ± 6%. The mean perfusion-metabolism mismatch (viability) scores were 5% ± 6% (of myocardium). Of these, 46% underwent revascularization based on PET viability data. Those who underwent revascularization and had higher perfusion-metabolism mismatch had fewer primary outcome events (cardiac death, MI, cardiac transplant or hospital stay due to unstable angina or heart failure). Those with perfusion-metabolism mismatch of <7% did not benefit from revascularization. Increasing creatinine and decreasing ejection fraction were also associated with increasing risk.

**Conclusions:** Patients with ischemic myocardial dysfunction and significant perfusion-metabolism mismatch (>7%) have better outcomes following revascularization.

**Reviewer's Comments:** This study showed that those who had increasing amounts of viable myocardium benefited the most from revascularization. The authors found a cut off value of 7% for viability, below which there was no benefit from revascularization. It should be kept in mind that viability is not dichotomous, but is rather a continuum. Thus in clinical decision making, a cut off value of 7% cannot be used as the sole value in deciding to proceed with revascularization without looking at the overall clinical picture. However, it seems reasonable that the greater the degree of viability, the more likelihood of functional recovery and good outcomes. The composite outcomes was largely driven by repeat hospital stays and was not powered to look at individual end points, such as death or MI. Prior observational studies have shown that at least 25% (as opposed to 7% in this study) of the myocardium needs to be viable to obtain clinical benefit from revascularization. This post hoc analysis needs to be validated in larger randomized clinical trials. (Reviewer-Anoop C. Parameswaran, MD).

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**Keywords:** Heart Failure, Viability, Fluorodeoxyglucose

**Print Tag:** Refer to original journal article
Exercise Intolerance Post-VALVE Surgery Largely Due to Muscular Weakness

Relationship Between Exercise Tolerance and Muscle Strength Following Cardiac Rehabilitation: Comparison of Patients After Cardiac Surgery and Patients With Myocardial Infarction.

Sumide T, Shimada K, et al:
J Cardiol 2009; 54 (October): 273-281

Lower limb muscle weakness contributes significantly to exercise intolerance in patients after VALVE surgery and may be ameliorated by combining aerobic exercise and resistance training.

Background: Numerous studies have undoubtedly established that cardiac rehabilitation (CR) improves muscle strength and exercise tolerance in patients after cardiac surgery and with MI. The association between strength and exercise tolerance following CR and the comparison of relationships among various patient diagnoses has not been entirely studied.

Objective: To examine the relationship between muscle strength and exercise tolerance in patients with MI and after cardiac surgery subsequent to CR.

Design: Observational cohort study.

Participants: 104 patients who participated in CR for 6 months after acute MI (n=34), post-coronary artery bypass grafting (CABG; n=42), post-cardiac valve surgery (VALVE; n=28).

Methods: All patients performed a symptom-limited cardiopulmonary exercise test before CR and at 6 months follow-up. Exercise tolerance, muscle strength, and thigh/calf circumferences were measured at baseline (4 to 11 days after surgery or acute MI onset) and then again 6 months after CR. Supervised exercise training, composed of a warm-up of 12 stretches, aerobic exercise for 60 minutes, resistance training of the abdominal, arm, and leg muscles, and a cool-down session, was performed once or twice a week for 6 months. In addition to the supervised exercise, patients were encouraged to perform home-based aerobic exercise twice weekly for at least 20 minutes.

Results: At 6 months, peak lower limb torques and peak oxygen uptake (VO\textsubscript{2}) increased in all groups (\textit{P} < 0.001), but there was no difference between groups. At baseline, thigh circumference was significantly smaller in the VALVE group as compared to the MI group. After 6 months, the thigh and calf circumferences significantly increased, and there were significant positive correlations between knee extensor torques and thigh circumferences, knee extensor torques and calf circumferences, and knee flexor torques and calf circumferences in the CABG and VALVE groups, but not in the MI group. A positive significant correlation between percent increases in peak VO\textsubscript{2} and muscular strength was observed in the VALVE group only (\textit{r} = 0.51; \textit{P} < 0.01). There were no significant differences in the number of supervised training sessions in each group.

Conclusions: Muscular weakness may cause exercise intolerance in patients after VALVE surgery.

Reviewer's Comments: Weakened lower limb muscles responded favorably to the CR program in all subjects, resulting in improved exercise tolerance, especially in the VALVE group. The duration of deconditioning was much longer in the VALVE group than the other patients in this study. Further studies are needed to assess whether increasing leg strength using resistance training could be effective for improving exercise intolerance in patients after heart valve surgery. (Reviewer-Debra L. Braverman, MD).

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Keywords: Cardiac Rehabilitation, Exercise Intolerance

Print Tag: Refer to original journal article
Although the baseline coronary artery calcium score correlates with the degree of coronary artery stenosis, individual vessels can have significant stenosis in the absence of calcification.

Background/Objective: The association between the degree of coronary artery calcification (CAC) and the degree of obstruction on a per-vessel basis is not well known. The aim of this study was to assess the relation between baseline CAC score by cardiac CT and subsequent anatomic findings on invasive coronary angiography.

Methods: 6,814 asymptomatic men and women participated in the Multi-Ethnic Study of Atherosclerosis (MESA). A total of 175 of these subjects subsequently underwent clinically indicated invasive coronary angiography in a span of 6 years. Data from these subjects were analyzed and reported.

Results: These 175 patients, in general, tended to be older, were more likely to be men, were Caucasian, and had a greater incidence of risk factors. For individual coronary arteries (except the left main coronary artery), there was a gradual increase in the baseline calcium score as the degree of stenosis increased. Of the 175 subjects with significant coronary artery stenosis (>75%), only 7 (4%) had a coronary artery calcium score of 0. However, when analyzing individual arteries, between 12% and 18% of coronary arteries had a calcium score of 0 despite significant coronary artery stenosis. 35% of those with >50% left main coronary artery stenosis had zero mass score in the left main artery, and 10% had a total CAC score of zero. As the CAC score severity increased, there was an increase in the number of diseased vessels. Results: The degree of baseline CAC is associated with the extent of obstructive coronary artery disease (CAD) in patients undergoing clinically indicated invasive coronary angiography. However, on a per-vessel basis, around 16% of vessels can have a zero calcium score despite significant coronary artery obstruction.

Reviewer's Comments: The presence of CAC is a powerful tool for risk stratification, and it provides incremental prognostic value over the Framingham score, especially in patients at intermediate risk for CAD. This study reinforces the excellent negative predictive value of a calcium score of zero. Of the 3,563 patients from the initial cohort who had a CAC score of zero, only 11 subjects (0.3%) ultimately had significant coronary artery stenosis. Even among the highly selected group of 175 patients who underwent clinically indicated coronary angiograms, only 4% had a CAC score of zero. It is important to note that although in this group of symptomatic patients the baseline calcium score was strongly associated with the degree of coronary stenosis, the relation was not so robust on a per-vessel basis. In fact, 12% to 35% of vessels with significant coronary artery stenosis had no calcification. Thus, while in a large asymptomatic cohort, the absence of CAC has an excellent negative predictive value, in patients with symptoms, the lack of coronary calcification should not be used to rule out significant obstructive CAD. (Reviewer-Anoop C. Parameswaran, MD).

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Keywords: Coronary Artery Calcium, Agatston, Coronary Computed Tomography

Print Tag: Refer to original journal article
Troponin T elevations are virtually universal post-CABG; if the correct cutpoint is identified, it may still have clinical usefulness.

**Background:** Coronary artery bypass grafting (CABG) can be associated with perioperative myocardial necrosis. Determining what level of biomarker release constitutes clinically significant damage can be difficult. Current guidelines suggest a level >5 times the 99th percentile of normal and new Q waves or left bundle-branch block (LBBB).

**Methods:** 847 patients undergoing isolated CABG were enrolled. Multiple clinical variables were collected. The occurrence of new Q waves or LBBB was assessed. Other outcomes were the need for vasopressors >24 hours postoperatively, postoperative heart failure, and all-cause 30-day mortality. Various cut points for cardiac troponin T (cTnT) were examined including >0.15 ng/mL (current guideline recommendation) and ≥1.60 ng/mL (based on a pilot study by the same authors).

**Results:** 99.4% of all patients had detectable cTnT levels; 96.6% had >0.15 ng/mL, while 36.7% had ≥1.60 ng/mL. Eight (0.9%) had new Q waves and 9 (1.1%) had new LBBB. A total of 85 patients experienced prolonged vasopressor requirements, heart failure, or death. The median cTnT for this group was 1.60 ng/mL, which was significantly higher than that for the uncomplicated group (1.01 ng/mL; interquartile range, 0.58 to 1.61; P <0.001). Separate examination of patients with preoperative MI versus those without preoperative MI showed no difference in the area under the receiver operating characteristic (ROC) curves for cTnT for the various outcome measures. In multivariate analysis, cTnT remained a significant predictor of death, heart failure, or vasopressor need.

**Conclusions:** Marked elevations of cTnT following CABG have prognostic value. In this retrospective study, 1.60 ng/mL was the optimal cut point for the prediction of serious early complications.

**Reviewer's Comments:** This study demonstrates several interesting and useful points. First, troponin T elevations are nearly universal post-CABG. Second, the current guidelines for diagnosis of perioperative MI in patients undergoing CABG are not very clinically useful. Third, similar to the case of B-type natriuretic peptide measurements in renal failure patients, appropriate adjustment of the cTnT cutpoint allows this biomarker to retain its predictive value. This study was retrospective and only looked at complications in the 30 days following surgery. It will be interesting to see if the authors' cutpoint of 1.60 ng/mL also predicts longer term complications. (Reviewer-Gregg S. Pressman, MD).