Hospitalists spend a significant portion of each day accessing and documenting in the electronic medical record, far more time than that spent with patients.

Background: The growth of hospitalists has been built on the hope that hospitalists can increase the quality and efficiency of care provided to hospitalized patients. How hospitalists achieve this efficiency and how they can further improve has not been well studied.

Objective: To better understand the work flow of hospitalists through continuous activity tracking of complete hospitalist shifts.

Participants/Methods: 24 hospitalists were followed for 2 full shifts on a non-teaching service in a tertiary care hospital. Direct observers electronically tracked minute-by-minute activities according to predefined categories. Because the hospitalist could be engaged in 2 tasks simultaneously, multi-tasking was recorded. The number of patients in the hospitalists’ care at the beginning of the day, the number of patients discharged, and the number of admissions were also tracked.

Results: 24 hospitalists were shadowed for 494 hours; however, due to multi-tasking, 537 hours of activity were observed. The hospitalists worked for an average of 10 hours per shift caring for 13 patients. Most of the time (34.1%) was spent accessing and documenting the electronic medical record (EMR). This averages about 4 hours per shift and included documentation, reviewing studies and notes, and placing orders. The next most time-intensive activity was communication, consisting of 25.9% of hospitalist time. Hospitalists communicated primarily with other physicians, but the time spent communicating with nurses, pharmacists, and other staff was also recorded. Time spent in direct care of patients made up 17.4% of physician time, accounting for approximately 2 hours per shift and 9 minutes per patient. Professional development, travel time, and personal time were all approximately 5% each. Increasing numbers of patients did not lead to decreased direct care per patient, but rather to decreased time spent on communication and documentation per patient.

Conclusions: Hospitalists spent the most time dealing with the EMR, followed by communication with other providers and staff, and then by direct patient care.

Reviewer’s Comments: The authors rightly point out that this study cannot only help hospitalists understand where they spend their time, but it may also help groups understand their inefficiencies on a larger scale. For example, the large amount of time spent with the EMR provides a huge opportunity to improve efficiency by improving access to computers, ease of documentation, and connectivity speed. Another potential area for improved efficiency is communication. Hospitalists often multi-tasked while trying to reach other providers, a potential sign that our modes of communication may be inefficient. Mobile phones, 2-way pagers, and handheld devices offer the opportunity to improve efficiency of communication. The hospitalist model is based on providing care that is both efficient and high quality. Understanding current hospitalists’ work flow and redesigning of systems to maximize efficiency could have a real benefit to both efficiency and the time spent in direct patient care. (Reviewer-Michelle Mourad, MD).

Keywords: Time in Motion, Hospitalists, Time Study

Print Tag: Refer to original journal article
Background: Guidelines recommend a systolic blood pressure (SBP) goal of <130 mm Hg for patients with diabetes (DM) to prevent microvascular and macrovascular complications. SBP treatment goals for patients with DM and coronary artery disease (CAD) are less clear.

Objective: To evaluate the impact of SBP control on cardiovascular outcomes in patients with DM and CAD.

Design/Participants: Observational, secondary data analysis from the International Verapamil SR-Trandolapril (INVEST) study, a multi-center prospective randomized trial comparing outcomes of patients with hypertension and CAD from 2000 to 2003.

Methods: Patients were randomly assigned to receive calcium channel blocker-based regimens (verapamil sustained release then angiotensin converting enzyme [ACE] inhibitor and/or a diuretic) or β-blocker-based regimens (atenolol then a diuretic and/or ACE). ACE inhibitors were recommended as part of the initial therapy for diabetic patients. The primary outcome was the first occurrence of all-cause mortality, non-fatal myocardial infarction (MI), or nonfatal stroke. Secondary outcomes were these occurrences individually. All INVEST patients aged >50 years with DM at baseline and CAD were categorized into 3 groups by average SBP: tight control (<130 mm Hg), usual control (130 to <140 mm Hg), or uncontrolled (>140 mm Hg). In the tight control group, SBP <130 mm Hg was further categorized in 5 mm Hg segments.

Results: 6400 patients were included. The mean age was 66 years; 54% were women; and the mean body mass index was 30. Thirty-five percent had tight control, 31% had usual control, and 34% were uncontrolled; ≥75% of patients in each group were taking ACE inhibitors. Patients with uncontrolled SBP were statistically more likely to experience adverse cardiovascular events (19.8%) than those with usual (12.6%) or tight control (12.7%); the adjusted hazard ratio (HR) was 1.46 (P <0.001). There were no significant differences in the risk of outcomes comparing tight and usual control. In a U.S. cohort of 5077 patients followed up for an extended period, all-cause mortality risk was greater with tight control (22.8%) than with usual control (21.8%) after adjustment (HR, 1.15; P =0.04). Patients with SBP <110 mm Hg compared with SBP 125 to 130 mm Hg also had significantly increased risk of all-cause mortality (HR, 2.18; P =0.02).

Conclusions: Tight SBP (<130 mm Hg) control in patients with DM and CAD does not appear to confer additional benefit in preventing adverse cardiovascular outcomes compared with SBP of 130 to 140 mm Hg.

Reviewer’s Comments: This is a large, well-conducted observational study of interest to hospitalists who care for many patients with DM and CAD. Results suggest that tight SBP control does not confer a preventive benefit above usual control and, over time, tight control may actually increase mortality risk. Additional study, particularly surrounding long-term potential risks of tighter control in this patient population, is warranted. (Reviewer-Anneliese M. Schleyer, MD).

Keywords: Blood Pressure Control, Cardiovascular Outcomes, Diabetes, CAD

Print Tag: Refer to original journal article
Antihypertensive Tx Status After Stroke May Not Affect Short-Term Outcome

Effects of Antihypertensive Treatment After Acute Stroke in the Continue or Stop Post-Stroke Antihypertensives Collaborative Study (COSSACS): A Prospective, Randomised, Open, Blinded-Endpoint Trial.

Robinson TG, Potter JF, et al:

Lancet Neurol 2010; 9 (August): 767-775

Antihypertensives in the first 2 weeks after stroke decrease blood pressure and do not increase adverse events, but may not affect stroke outcome or mortality.

Background: Hypertension is a risk factor for stroke, and many stroke patients are on antihypertensive therapy. Both hypertension and hypotension hold the potential to worsen stroke outcomes. It is unclear whether antihypertensive therapy should be continued in the immediate post-stroke period.

Objective: To measure the efficacy and safety of continuation of antihypertensive medications after stroke.

Design: Multicenter, prospective, randomized, open, blinded-end point trial.

Methods: Patients were randomized to receive or discontinue pre-existing antihypertensive medications for the 2 weeks after stroke. Other aspects of clinical care management were determined by the primary physician. Baseline assessments of stroke classification and blood pressure were performed. Outcomes at 2 weeks and 6 months were assessed by investigators blinded to treatment assignment. The primary end point was death or dependency at 2 weeks. Secondary outcomes at 2 weeks included neurological and functional status, blood pressure change, discharge destination and serious adverse events, and 6-month mortality, stroke recurrence, quality of life, and residence.

Participants: Adults with confirmed mild to moderate, non-dysphagic acute stroke (infarction or primary hemorrhage) on antihypertensive drugs who had received their last dose within 48 hours of randomization.

Results: The trial was stopped for lack of subjects and funding before achieving target recruitment. Of the 763 patients randomized, 706 completed the study. The mean age was 74 years. Mean blood pressure was 150/81 mm Hg. The majority of strokes were ischemic. There was no difference in the groups at baseline. The groups did not differ in the primary outcome at 2 weeks but when adjusted for age, the primary outcome was more common in those >75 years. The group receiving antihypertensives had a mean change in systolic blood pressure of -13 mm Hg. At 6 months, in the cohort of patients with ischemic stroke, there was a relative risk reduction of 0.70 in the primary outcome for those receiving antihypertensives.

Conclusions: Continuing antihypertensives did not decrease adverse stroke outcomes at 2-week or 6-month mortality, but the study was underpowered to detect a difference.

Reviewer’s Comments: This study is not conclusive enough to make firm recommendations or change guidelines. Continuing therapy was not found to be dangerous from a safety standpoint, but neither was the associated decrease in blood pressure found to be associated with improved outcomes. Because the study selected only patients with low stroke scores and less severe strokes and those who were not dysphagic, we cannot extrapolate to more severe or dysphagic strokes. Furthermore, there may be differences between antihypertensive medication classes, which were not appreciated here. (Reviewer-Jennifer Best, MD).

Keywords: Stroke, Secondary Prevention

Print Tag: Refer to original journal article
Antipsychotics May Be Associated With Development of Pneumonia in Elderly

Association of Community-Acquired Pneumonia With Antipsychotic Drug Use in Elderly Patients: A Nested Case-Control Study.


The current use of typical or atypical antipsychotics is associated with an increased risk of community-acquired pneumonia in elderly patients.

**Background:** Some recent epidemiologic studies have shown an association between antipsychotic use in the elderly and the development of pneumonia.

**Objective:** To investigate whether typical or atypical antipsychotic use is associated with pneumonia in elderly patients.

**Design:** Large database case-control study.

**Methods/Participants:** From 1996 to 2006, all patients aged ≥65 years who received a prescription for an antipsychotic medication were included. From this cohort, cases were those who were diagnosed with community-acquired pneumonia (CAP) during the study (each case was specifically evaluated for the diagnosis). Controls were new users of antipsychotics who did not develop pneumonia and who were matched by age, sex, and date.

**Results:** 2560 patients were prescribed antipsychotics, primarily for behavioral symptoms of dementia, anxiety disorders, or other psychiatric disorders. Two-hundred sixty-four patients were diagnosed with pneumonia. The current use of atypical antipsychotic drugs (OR, 2.61; 95% CI, 1.48 to 4.61) or typical antipsychotic drugs (OR, 1.76; 95% CI, 1.22 to 2.53) was associated with an increased risk of CAP compared to the past use of antipsychotics. Only atypical antipsychotics were associated with fatal pneumonia (OR, 5.97; 95% CI, 1.49 to 23.98). The risk was highest soon after starting treatment and increased with increasing doses. In subgroup analysis, phenothiazines as a class and risperidone had the highest risk for CAP.

**Conclusions:** In a large database, the current use of typical or atypical antipsychotics was associated with development of CAP. The mechanism is not completely clear but may be related to H₁-receptor blocking, leading to sedation and aspiration. Further studies are needed.

**Reviewer's Comments:** This large and well-performed database analysis confirms previous data showing an association between the use of antipsychotics in elderly patients and the development of CAP. Should we stop antipsychotic use in all of our elderly patients? Probably not, as often these are the best agents to help manage delirium or behavioral symptoms on dementia. However, as providers, we should be aware that these drugs and atypical antipsychotics have risks and, we must weigh the risk-to-benefit ratio. (Reviewer-Bradley A. Sharpe, MD).

Keywords: Community-Acquired Pneumonia, Antipsychotics, Elderly Patients

Print Tag: Refer to original journal article
Treatment of pneumonia may prolong survival in persons with advanced dementia, but more aggressive care is associated with more discomfort.

**Background:** Nursing home (NH) residents with advanced dementia are often treated with antimicrobials and/or are hospitalized when they develop pneumonia. The impact of antimicrobial therapy and hospitalization on survival and comfort is not well known.

**Objective:** To assess the impact of antimicrobial therapy for pneumonia on outcomes in NH patients with advanced dementia.

**Design:** Data analysis from a large, multisite, prospective cohort study of NH residents with dementia (the Choices, Attitudes, and Strategies for Care of Advanced Dementia at the End-of-Life [CASCADE]) recruited from 22 NHs in a single U.S. urban area.

**Participants/Methods:** Patients aged ≥60 years with dementia and severe cognitive impairment by the Cognitive Performance Score and Global Deterioration Scale score were recruited. All participants had to have designated health care proxies and speak English. Patients were followed for 18 months or until death; proxies were interviewed at baseline and quarterly. Primary outcomes were survival (days) and comfort (by Symptom Management at End-of-Life in Dementia [SM-EOLD] scale).

**Results:** 133 patients had at least 1 episode of pneumonia; in total these patients had 225 pneumonia episodes. Participants had a mean age of 86 years, 81% were women, 92% were Caucasian, and 44% lived in special care dementia units. Among the 225 pneumonia episodes, 91% were treated with antimicrobials (55% oral, 16% intramuscular, and 20% IV or hospitalization) or were hospitalized. Antimicrobial therapy (any route) was associated with lower mortality compared to no treatment (adjusted hazard ratio, 0.2 to 0.26). The average adjusted increase in survival was 273 days. There were no statistically significant differences between routes of administration and survival. Comfort was greater among patients who received less aggressive care (no antibiotics, oral antibiotics).

**Conclusions:** Treatment of pneumonia in NH patients with dementia may improve survival but at the detriment of comfort.

**Reviewer’s Comments:** This is a well-designed study of patients clearly identified as having severe dementia who are of significance to many hospitalists who often work with patients with dementia and their caregivers. Results highlight the need to understand the goals of care for every patient; oral antibiotics may offer a balance between improving survival without compromising patient comfort. Study generalizability is limited by the observational nature of the study conducted in a single urban area and with an English-speaking population. Additional study in different populations is warranted, as well as examination of outcomes relative to appropriateness of specific antimicrobial therapy. (Reviewer-Anneliese M. Schleyer, MD).

**Keywords:** Pneumonia, Antimicrobial Therapy, Dementia

**Print Tag:** Refer to original journal article
Passengers of advanced age, with altered mental status or with in-flight automated external defibrillator use, are at increased risk for medical emergencies becoming flight diversions or in-flight deaths.

**Background:** Medical emergencies challenge clinicians as we lack our usual diagnostic and treatment modalities and are costly and inconvenient when they result in flight diversions.

**Objective:** To provide a current description of in-flight medical emergencies and to examine predictors of flight diversions and in-flight deaths.

**Methods:** The authors looked at a retrospective cohort of 4068 medical emergencies on commercial airlines over a 5-year period (2003 to 2008). All flights where a satellite phone was used to seek medical advice were counted. The authors looked at the frequencies and the causes of medical emergencies and looked for variables associated with flight diversions and in-flight deaths.

**Results:** Of the 4068 medical emergencies, 46 were diversions and 30 were deaths, giving an incidence of 11.63 medical emergencies, 0.13 diversions, and 0.09 deaths per billion revenue passenger kilometers. Increasing age, altered mental status, and use of the in-flight automated external defibrillator (AED) all placed passengers at higher risk for diversion and death. Unconsciousness was the strongest risk factor conferring a 33-fold increase in diversion and a 234-fold increase in death. Neurologic problems (39.1%), cardiac problems (23.9%), and obstetrical and/or gynecologic problems (13.0%) accounted for most of the diversions. Cardiac problems accounted for only 6% of all emergencies, but 23.9% of diversions and 66.7% of all deaths. AED use was rare, used in only 23 (0.6%) of the 4068 medical emergencies, but conferred a poorer prognosis, being deployed in 63% of deaths.

**Conclusions:** Passengers with advanced age or altered mental status and those for whom an AED is used during a medical emergency are at increased risk for flight diversion or death.

**Reviewer’s Comments:** As physicians called upon to assess a patient, it is helpful to know which patients may have a poorer prognosis. The relative risk of the unconscious patient caused the authors to recommend that in-flight personnel be trained in the assessment of consciousness level to more closely be able to anticipate serious changes in sensorium. The authors also suggested that more rigorous pre-flight screening might reduce the numbers of in-flight emergencies, diversions, and deaths. One might also look to the AED results and wonder about the benefit and appropriate use of AEDs on a plane. It is troubling that only 1 patient for whom an AED was used required a shock, and notable that AEDs were used in only 63% of deaths. Perhaps more widespread use of AEDs would have revealed more shockable rhythms. This brief report is a good first step in examining the predictors of in-flight diversions and in-flight deaths. I would be interested in further studies that look at more objective data of the types of illnesses found either at the receiving hospital or on autopsy. (Reviewer-Michelle Mourad, MD).

**Keywords:** Medical Emergencies, In-Flight

**Print Tag:** Refer to original journal article
In stable patients with mild chronic obstructive pulmonary disease, a hypoxic challenge increases coagulation activation and systemic inflammation.

**Background:** Patients with chronic obstructive pulmonary disease (COPD) have an increased risk of venous thromboembolism (VTE). It is not definitively known whether hypoxia or increased systemic inflammation, particularly during acute exacerbations, contributes to hypercoagulability and increased VTE risk.

**Objective:** To assess the impact of hypoxia on coagulation factors and systemic inflammation in COPD.

**Design:** Single-blind, placebo-controlled trial.

**Participants/Methods:** Patients with COPD, with forced expiratory volume in 1 second (FEV₁) >50% of predicted and who were clinically stable (no antibiotics or steroids) were randomized to medical air (controls) or 100% nitrogen via 40% face mask at 10 L/min (hypoxia group), similar to conditions in airplanes at high altitude. Patients with heart disease, malignancy, hypercoagulability, a history of VTE, or those requiring supplemental oxygen chronically or oral/inhaled steroids were excluded. Vital signs were measured at baseline and then every 30 minutes. Blood samples were taken at baseline and after 2 hours to measure thrombin antithrombin complex (TAT), prothrombin activation fragments (F1+2), D-dimer, von Willebrand factor antigen (VWF:Ag), and interleukin-6 (IL-6).

**Results:** 20 patients were recruited. Among the controls, vital signs and coagulation markers did not change over the 2-hour study period. In the hypoxia group, heart rate was greater and oxygen saturation was lower at the end of the study ($P < 0.05$). Mean TAT ($P < 0.001$), F1+2, and IL-6 (both $P < 0.01$) increased after 2 hours of hypoxia, while D-dimer and VWF:Ag did not change statistically.

**Conclusions:** Hypoxia appears to increase coagulation activation and systemic inflammation in patients with COPD. This may contribute to increased VTE risk during acute exacerbations or other times of relative hypoxia. It remains unknown whether VTE risk may be heightened further in a hypobaric environment (airplanes at high altitude). The role of supplemental oxygen also needs further study.

**Reviewer's Comments:** This is an interesting, very small study that suggests that there may be an association between hypoxia, coagulation activation, and systemic inflammation in mild COPD. Notably, patients on steroids (oral or inhaled) were excluded significantly limiting generalizability to many inpatients that hospitalists care for. The authors suggest that this association may make consideration of VTE prophylaxis even more important; this study was supported in part by a pharmaceutical company that manufactures heparin products. (Reviewer-Anneliese M. Schleyer, MD).

**Keywords:** Hypercoagulability, Hypoxia, COPD

**Print Tag:** Refer to original journal article
Oral Steroids as Good as IV Steroids for COPD Exacerbation

Association of Corticosteroid Dose and Route of Administration With Risk of Treatment Failure in Acute Exacerbation of Chronic Obstructive Pulmonary Disease.

Lindenauer PK, Pekow PS, et al:

JAMA 2010; 303 (June 16): 2359-2367

Treatment failure in hospitalized patients with chronic obstructive pulmonary disease exacerbation is no more common with oral steroids, which also have beneficial effects for cost and length of hospital stay, than with IV steroids.

**Background:** Corticosteroid dosing in acute exacerbations of chronic obstructive pulmonary disease (AECOPD) is highly variable, and the optimal approach is unknown.

**Objective:** To determine the relative efficacy of oral and IV corticosteroids for patients hospitalized with AECOPD.

**Design:** Retrospective cohort study.

**Participants:** 79,985 patients with AECOPD who were admitted to acute care and treated with systemic corticosteroids within the first 2 days of admission at 414 U.S. hospitals were included. Patients with secondary pulmonary diagnoses, as well as those who received outlier doses of steroids, were excluded.

**Methods:** Data regarding demographics, steroid treatment and use of other COPD medications, hospital and pharmacy costs, comorbidities, and outcomes were obtained from a large network database. The primary end point was a composite outcome of treatment failure.

**Results:** Most patients (92%) were treated with IV steroids initially. There were no differences between hospital death or treatment failure between the groups. Following adjustment, oral therapy did not differ from IV therapy; furthermore, treatment failure in matched analysis was less common for oral steroids, as was length of stay and overall hospital cost.

**Conclusions:** Hospitalized AECOPD patients on oral corticosteroids do not have higher rates of treatment failure compared to those on IV.

**Reviewer's Comments:** Current practice in steroid management of AECOPD appears to deviate from guidelines, which do not recommend first-line, high-dose IV steroids. Based on this large study, hospitalists may feel assured that using oral corticosteroids as initial therapy for patients with AECOPD is just as good as IV therapy and may have other benefits. These results do not apply to those requiring critical care or mechanical intubation or those with secondary diagnoses. (Reviewer-Jennifer Best, MD).

**Keywords:** COPD, Corticosteroids, Acute Exacerbation, Treatment

Print Tag: Refer to original journal article
Audible gurgling sounds during quiet respiration or talking are predictive of the development of hospital-acquired pneumonia.

**Background:** Hospital-acquired pneumonia (HAP) is a morbid condition that can result in prolonged hospital stay and increased mortality.

**Objective:** To determine whether patients with gurgling sounds heard during speech or quiet breathing were more likely to develop HAP.

**Methods:** Over a 4-month period, all patients admitted to the medicine or respiratory units were examined daily for airway gurgling. To meet criteria for gurgling, patients had to have gurgling heard with or without a stethoscope during quiet breathing or speech at any point during their hospital stay. The first consecutive 20 patients with gurgling were enrolled along with 60 patients without gurgle who were admitted to the same ward on the same day. Multivariate analysis was used to assess the contribution of gurgle after adjustment for other demographic, physiologic, and outcome variables.

**Results:** 20 patients with gurgling were compared to 60 patients without gurgling. Patients with gurgle were found to be older (78.5 years vs 65.2 years), were more likely to have dementia (70% vs 13%), and more likely to have been admitted from a nursing home (75% vs 6%). After controlling for other predictors, dementia and recent treatment with opiates were independent predictors of gurgling. HAP occurred in 55% of patients with a gurgle compared to 1.7% of patients without. After adjustment for age, dementia, opiate use, stroke, and Charlson score, gurgling emerged as the sole independent predictor of HAP (OR, 140.1) and ICU transfer (OR, 35.1).

**Conclusions:** During quiet breathing or speech, if gurgling sounds are heard audibly or with a stethoscope, patients are at increased risk for HAP.

**Reviewer's Comments:** Patients who gurgled were 140 times more likely to get HAP after multivariate analysis. Gurgling patients were also more likely to require a transfer to the ICU during their stay. This simple, relevant study demonstrates that in this patient population, gurgling is predictive of HAP. Though these results should be viewed with caution given the small sample size and the single-site design, the results are biologically plausible. If these results are confirmed, efforts should then turn to working with these patients to promote cough and minimize secretions. (Reviewer-Michelle Mourad, MD).

Keywords: Hospital-Acquired Pneumonia, Gurgling

Print Tag: Refer to original journal article
AMA Discharges Can Be Deadly for Your Patients

Leaving Against Medical Advice (AMA): Risk of 30-Day Mortality and Hospital Readmission.
Glasgow JM, Vaughn-Sarrazin M, Kaboli PJ:

J Gen Intern Med 2010; 25 (9): 926-929

Hospitalists and hospitals are advised to consider interventions targeting patients who discharge against medical advice in an effort to improve outcomes.

**Background:** Discharges against medical advice (AMA) are not uncommon in many hospital settings and place patients at risk of adverse outcomes. However, the specific risks of an AMA discharge for the general medical population are unknown.

**Objective:** To determine hospital readmission and mortality rates and identify patient risk factors associated with AMA discharges.

**Design:** Retrospective cohort study.

**Methods:** Patient demographics, diagnoses, admission and discharge dates, discharge disposition, and death data were obtained from Veterans Administration (VA) databases. The primary outcome was readmission to a VA medical center or mortality within 30 days of discharge. Non-AMA and AMA cohorts were compared statistically. Hazard models were constructed to identify risk factors for readmission and death.

**Participants:** 1,930,947 medical patients discharged from 1 of 129 VA medical centers were included. Excluded were those discharged to a skilled nursing facility or a "nonstandard" setting and those who died while hospitalized.

**Results:** 1.7% of patients were discharged AMA; these patients were younger, were more commonly black, and were low-income. As compared to non-AMA discharges, AMA patients had higher 30-day rates of readmission (17.7% vs 11.0%; \( P < 0.001 \)) and mortality (0.75% vs 0.61%; \( P = 0.001 \)). In hazard models for readmission, AMA discharge (HR, 1.35), age, income, 5 medical comorbidities, and non-white race were identified as risk factors. Alcohol, congestive heart failure, chronic obstructive pulmonary disease, anemia, complicated diabetes mellitus, lymphoma, and metastatic cancer were found to be protective. In a model targeting only AMA discharges, no risk factors were found. Age, alcohol, congestive heart failure, and neurologic disease were protective. In hazard modeling for mortality, AMA discharge was associated with a non-significant increase in risk. Age and 7 medical comorbidities increased risk.

**Conclusions:** AMA discharge places patients at higher risk of readmission and mortality at 30 days.

**Reviewer's Comments:** This was a VA study and may not be generalizable, but its message of increased risk is an important one. While we cannot do a lot about the characteristics of a given patient who decides to leave AMA, what we do after he or she leaves is under our control. Interventions such as follow-up phone calls, home visits, or attempts to schedule a follow-up prior to discharge should be implemented and studied. At a minimum, careful counseling regarding the risk of leaving the hospital is a must. Each of us should know our hospital's population, including those patients who have these risk factors and those with a history of AMA discharge. Not surprisingly, previous research has shown that prior AMA discharge is itself a risk factor. (Reviewer-Jennifer Best, MD).

Keywords: Hospital Discharge, Discharges Against Medical Advice, Mortality, Morbidity

Print Tag: Refer to original journal article
Is CABG Surgery Superior?

Ten-Year Follow-Up Survival of the Medicine, Angioplasty, or Surgery Study (MASS II): A Randomized Controlled Clinical Trial of 3 Therapeutic Strategies for Multivessel Coronary Artery Disease.

Hueb W, Lopes N, et al:

Circulation 2010; 122 (September 7): 949-957

Bypass surgery is superior to medical therapy or percutaneous intervention in rates of revascularization or myocardial infarction at 10 years.

**Background:** There remains controversy about the optimal management strategy for patients with stable multivessel coronary artery disease (CAD) and preserved left ventricular function. Medical therapy (MT), percutaneous intervention (PCI) and bypass surgery (CABG) all have some data to support them; however, the available data are all <5 years follow-up.

**Objective:** To report the 10-year follow-up of the Medicine, Angioplasty, or Surgery Study (MASS II). Five-year follow-up had demonstrated a significant benefit in end points of revascularization, but no change in mortality for CABG versus the other treatment modalities.

**Methods:** The MASS trial is reported elsewhere, but is a single-center study of patients with >70% stenosis of multiple proximal coronary arteries with ischemia by stress testing. Patients all received optimal medical therapy, and were excluded if they had refractory angina, myocardial infarction (MI) requiring revascularization, ejection fraction (EF) <40%, or left main coronary artery stenosis ≥50%, as well as other standard comorbid cardiac conditions. Patients were followed every 6 months for 10 years, including exercise testing annually. Primary end points were total mortality, Q-wave MI, refractory angina requiring revascularization, with secondary end points of angina or death due to a cardiac cause or cerebrovascular accident. PCI was performed with bare metal stents in the majority of patients.

**Results:** 611 patients from 1995 to 2000 were enrolled, with average follow-up of 11.4 years (9 to 15) and were appropriately matched at baseline. At 5- and 10-year follow-up, there was a significant difference in cumulative event-free survival (overall mortality, unstable angina requiring revascularization, or Q-wave MI). There was no difference between the PCI and MT group, but there was a protective effect of CABG compared with MT and PCI (HR, 0.43 and 0.53, respectively). There was no statistically significant difference in cumulative mortality among the 3 groups.

**Conclusions:** CABG was associated with a lower incidence of combined event-free survival compared with PCI or MT and specifically a lower rate of revascularization, MI, and cardiac death when compared with MT, and a lower rate of revascularization, MI, and persistent angina when compared with PCI.

**Reviewer’s Comments:** Many specific aspects of MT and PCI have evolved during the study and follow-up period, but this study would make an argument for consideration of revascularization, particularly CABG, as initial treatment strategy for patients with multivessel CAD and preserved EF. It should be noted that even in MT patients, nearly 70% were alive at 10 years and 40% of them free of MI or revascularization. (Reviewer-Karen Stout, MD).

**Keywords:** Coronary Artery Disease, Revascularization, Medical Therapy

**Print Tag:** Refer to original journal article
Calcium Supplementation Associated With Increased Risk of MI

Effect of Calcium Supplements on Risk of Myocardial Infarction and Cardiovascular Events: Meta-Analysis.

Bolland MJ, Avenell A, et al:

BMJ 2010; 341 (July 29): c3691

Calcium supplementation over 800 mg per day is associated with a 30% increased risk of first-time myocardial infarction.

Background: With and without our advice, millions of Americans take calcium supplementation as awareness about osteoporosis prevention increases. The only caution we give is about risk for constipation and the binding of other medications, but are there other risks?

Objective: To assess whether calcium supplements are associated with higher cardiovascular events.

Design: Meta-analysis.

Methods: Studies were searched from 1966 to 2010, and included randomized placebo-controlled trials of adults (mean age, >40 years) taking at least 500 mg of calcium per day. Trials were >1 year, included both genders, and had >100 participants. Trials that combined vitamin D and calcium in the study group and no vitamin D in the placebo group or where subjects had a major disease other than osteoporosis were excluded. Patient level and trial level data were obtained for the primary end points of time to first myocardial infarction (MI), stroke (CVA), or a composite of MI, CVA, and sudden death; secondary end point was time until death (all-cause mortality).

Results: A meta-analysis was conducted in the usual fashion and models were assessed with covariates including usual cardiovascular risk factors. Fifteen trials were included, 5 with patient-level data and 10 with trial-level data. Calcium supplementation was associated with an increased risk for first-time MI. Patient-level data showed 143 MIs in the calcium group and 111 in the placebo group (HR, 1.31; CI, 1.02 to 1.67; \( P = 0.035 \)), with a number needed to harm (NNH) of 69. This was dose-related with dietary intake >805 mg/day (HR, 1.85; CI, 1.28 to 2.67) and no association below that level. Recurrent cardiovascular events were also higher in the calcium arm. Patient-level data showed non-significant increased risk for CVA (HR, 1.2; CI, 0.96 to 1.50; \( P = 0.11 \)), the composite end point (HR, 1.18; CI, 1.0 to 1.39; \( P = 0.057 \)), and all-cause mortality (HR, 1.09; CI, 0.96 to 1.23; \( P = 0.18 \)). Trial level data showed increase risk for MI in the calcium arm (RR, 1.27; CI, 1.01 to 1.59; \( P = 0.038 \)), but not stroke, composite, or all-cause mortality.

Conclusions: Calcium supplemtations are associated with an increased risk of MI.

Reviewer’s Comments: This study highlights the concern that calcium supplements may via calcium deposition in blood vessels increase the risk for cardiovascular events. Current evidence shows an "at best" modest decrease in fracture risk with calcium supplementation in contrast with NNH of 69 for MI. This appears dose-related but not clearly linear, and not affected by traditional risk factors for cardiovascular events. So is recommending calcium in any form safe? Assessing for a similar association with dietary calcium intake would be important. The low NNH makes assessment of MI a plausible secondary outcome in the next randomized controlled trial of calcium supplementation. For now, I plan to caution patients about calcium supplementation above 500 mg daily, but will continue to recommend vitamin D. (Reviewer-Genevieve L. Pagalilauan, MD).

Keywords: Calcium Supplementation, Cardiovascular Events, Myocardial Infarction

Print Tag: Refer to original journal article
Cardiac imaging accounts for significant radiation exposure, which is higher in men and increases with age.

**Background:** Use of cardiac procedures using ionizing radiation, such as myocardial perfusion imaging (MPI) and cardiac CT, have increased in recent decades; however, there is concern about radiation exposure as a consequence of these procedures.

**Objective:** To describe the cumulative effective radiation exposure due to cardiac procedures in a general population and to identify those patients at increased risk for high radiation exposure.

**Methods:** Adults aged 18 to 64 years were analyzed through an administrative claims database in 5 healthcare markets with similar demographics (Arizona, Dallas, Orlando, South Florida, Wisconsin) administered by United Healthcare. Cardiac imaging procedures were identified, including myocardial perfusion imaging, cardiac catheterization, electrophysiology procedures, cardiac CT, and radionuclide blood pool imaging. Radiation exposure was described by 2 thresholds, either >3 mSv/year, which is the background radiation exposure for an adult in the U.S. or >20 mSv/year, which is the upper limit of occupational exposure for at-risk workers, averaged over 5 years. Published estimates of radiation doses were used to calculate the dose/procedure.

**Results:** 952,420 patients from 2005 to 2007 were assessed, with mean age of approximately 36 years with 52% women. About 90,000 patients (9.5%) underwent at least one cardiac procedure during the study period. The numbers of cardiac procedures increased with age and were more frequent in men. Half of the imaging procedures occurred in physician offices, including the majority of MPI and CT, while the remainder occurred in inpatient settings and hospital-based outpatient settings. The largest contributor to overall effective radiation dose was MPI (74%), with cardiac catheterization next (21%). Overall, 89.0 of 1000 patients had radiation doses of 3 to 20 mSv/year, while 3.3 of 1000 had >20 mSv/year. Radiation exposure increased dramatically with age and was higher in men, with the highest radiation exposure seen in the health care markets in Orlando and South Florida, even after adjustment for age and gender.

**Conclusions:** Cardiac imaging procedures result in substantial radiation exposure in many patients in the U.S.

**Reviewer’s Comments:** Improved diagnosis and treatment modalities for heart disease have resulted in a marked increase in radiation-related cardiac procedures, and the aggregate radiation of those procedures may not be benign. Data such as this suggest the need to modify protocols and treatment recommendations that consider the lifetime radiation exposure of patients, if we are to avoid the complications of radiation-related disorders as a consequence of cardiac imaging. The study also confirms that the majority of radiation-related imaging procedures are occurring in physician offices, and that there is geographic variation warranting further study. (Reviewer-Karen Stout, MD).

Keywords: Cardiac Imaging, Ionizing Radiation, Cumulative Exposure

Print Tag: Refer to original journal article
Background: Metformin, an oral hypoglycemic agent, has carried the concern for lactic acidosis ever since an earlier biguanide, phenformin, was withdrawn from the market due to increased risk for lactic acidosis (40 to 60 cases per 100,000 patient-years). As such, people with conditions that concurrently increase risk for lactic acidosis including cardiovascular, pulmonary, hepatic, and renal disease, as well the elderly are cautioned against use of metformin.

Objective: To assess incidence of nonfatal and fatal lactic acidosis and blood lactate levels compared to placebo or non-metformin arms in subjects with type 2 diabetes.

Design: Systematic review of prospective and observational cohort studies.

Methods: A comprehensive search for trials of metformin use in type 2 diabetes patients was conducted including a metformin arm for at least 1 month compared to placebo or a non-metformin diabetes medication. Studies were assessed with a Jadad quality score, as well as Chi-square analysis and funnel plots for heterogeneity. Pooled data were expressed as a risk difference between the metformin arm and the placebo/non-metformin arm, and results were further conveyed as number needed to harm and relative risk versus the comparison group.

Results: Of the 347 articles that met inclusion criteria, 209 were prospective comparative studies, 125 prospective cohort, and 13 retrospective trials. Overall, 69,642 subjects were in the pooled metformin arm, and 26,653 in the non-metformin arm. The average age was 57 years and 61% were men; renal (Cr >1.5), hepatic, and cardiovascular disease were excluded from individual studies about 50% of the time. In the 70,490 patient-years of the pooled metformin group, there were no cases of fatal or nonfatal lactic acidosis. Using Poisson statistics, the upper limit for the incidence of metformin-related lactic acidosis was 4.3 of 10,000 patient-years, and for the non-metformin group, 5.4 of 10,000 patient-years. There were insufficient data from the original studies to do subgroup analysis on individual hypoxemic conditions, but >50% of studies allowed ≥1. There was no difference in the net lactic acid levels between groups.

Conclusions: There is no evidence based on prospective comparative trials or observational cohort studies that metformin increases the risk for lactic acidosis compared to any other antihyperglycemic medication.

Reviewer's Comments: This trial helps to debunk a long-standing medical myth that metformin is absolutely contraindicated in hypoxic conditions. Weighing the potential 50% mortality benefit shown in the U.K. Prospective Diabetes Study for obese type 2 diabetes patients with solo-agent use of metformin, the potential harm that may be hidden from this rigorous systematic review seems overwhelmingly outweighed. I would still be cautious about use in patients with marked renal insufficiency or multiple hypoxic comorbidities until those groups could be studied in a more targeted fashion. (Reviewer-Genevieve L. Pagalilauan, MD).

Keywords: Metformin, Adverse Reactions. Lactic Acidosis, Type 2 Diabetes Mellitus

Print Tag: Refer to original journal article
Low-carbohydrate diets using vegetable proteins have lower mortality than those using animal proteins.

**Background:** Low-carbohydrate diets are demonstrated to promote weight loss, but the data are conflicting on the effect on lipids. There are also no data on the long-term mortality of a low-carbohydrate diet, particular stratifying based on protein source.

**Objective:** To report the effect of low-carbohydrate diets on mortality, overall and cause-specific, in 2 large cohorts.

**Methods:** The authors report data from the Nurse's Health Study (NHS) and from the Health Professional's Follow-up Study (HPFS). Each study was described previously. At enrollment, the NHS included women aged 30 to 55 years and the HPFS followed men aged 40 to 75 years. The NHS food frequency questionnaire (FFQ) was sent in 1980, and expanded in subsequent years. Similarly, a FFQ was sent in the HPFS and follow-up was >90% in each cohort. Participants were included if they had complete FFQ and plausible caloric intake. Those with cancer or heart disease at baseline were excluded. Over 85,000 women and 44,500 men were included. Low-carbohydrate scores were used and described in previous studies. In addition, a vegetable low-carbohydrate score and an animal low-carbohydrate score was derived and usual covariates were assessed. Deaths were ascertained from the National Death Index, families, and the postal service and the cause of death was obtained from review of medical records, categorized as cardiovascular disease or different types of cancer. The study was funded by the National Institutes of Health.

**Results:** The NHS had 26 years of follow-up and the HPFS had 20 years. Men and women with higher overall and animal carbohydrate scores were associated with higher body mass index and were more likely to be smokers, while those who had higher vegetable carbohydrate scores were more likely to drink alcohol and eat whole grains. After adjustment, there was a statistically higher risk for all-cause mortality for the animal low-carbohydrate score (HR, 1.23) when comparing extremes of intake when grouped in deciles. The animal low-carbohydrate score was also associated with higher cardiovascular disease and cancer mortality (HR, 1.14 and 1.28, respectively). The higher vegetable low-carbohydrate score was associated with lower all-cause and cardiovascular disease mortality (HR, 0.8 and 0.77, respectively).

**Conclusions:** An animal-based low-carbohydrate diet was associated with higher all-cause mortality in men and women while a vegetable-based low-carbohydrate diet was associated with lower all-cause and cardiovascular disease mortality.

**Reviewer's Comments:** There remains enthusiasm for different forms of low-carbohydrate diet, with little long-term data regarding the overall health effects of these diets. This study would suggest that a low-carbohydrate diet should rely on vegetable proteins rather than animal proteins. This does not reflect any specific marketed diet. The socioeconomic and insurance advantages of the study populations likely do not generalize well to the population as a whole. (Reviewer-Karen Stout, MD).

Keywords: Low-Carbohydrate Diet, Cardiovascular Mortality, Cancer Mortality

Print Tag: Refer to original journal article
Lung Cancer Screening With CT, CXR May Lead to False Positives

Cumulative Incidence of False-Positive Test Results in Lung Cancer Screening: A Randomized Trial.
Croswell JM, Baker SG, et al:
Ann Intern Med 2010; 152 (April 20): 505-512

Background: Despite current lack of clear evidence to support a mortality benefit from lung cancer screening, there is direct-to-consumer promotion of screening modalities (particularly low-dose chest CT) that leads patients to request CT or other imaging tests.

Objective: To determine the rates of false-positive tests and unnecessary diagnostic procedures generated by 2 years of lung cancer screening using either low-dose chest CT or chest x-rays (CXR).

Design/Participants: Randomized, controlled trial of 3190 current or former smokers (aged 55 to 74 years) with ≥30 pack-years of cigarette exposure and no history of lung cancer. Subjects were recruited from 6 U.S. communities as part of the Lung Cancer Screening Study from September 2000 to January 2001. Participants were excluded if they had a chest CT within 24 months of enrollment, had previous removal of a portion of lung, had quit smoking >10 years previously, or had any malignancy (except non-melanoma skin cancer).

Methods: Participants were randomized to either low-dose chest CT or posteroanterior CXR at baseline and at 1 year, with 1-year of clinical follow-up after the final screening. A positive CT exam was defined by the presence of a noncalcified nodule ≥4 mm or radiologist concern for malignancy based on the following: spiculated, noncalcified nodule of any size; focal parenchymal opacification; endobronchial lesion; hilar, mediastinal, bony, or pleural mass; or major atelectasis. Positive CXRs were defined by the presence of a nodule with circular opacity ≤3 cm in diameter; a mass >3 cm; hilar or mediastinal lymph node enlargement (excluding calcified nodes); or major atelectasis, infiltrates, consolidations, or pleural masses suggestive of cancer. Positive results were communicated to the participant and his or her physician. There was no specific algorithm for follow-up of positive results, but physicians could ask study personnel for recommendations. Suspicious radiographic findings were not always biopsied. False-positive screenings were defined as a positive screening test with subsequent negative work-up or ≥12 months of follow-up with no lung cancer diagnosis.

Results: 59% of participants were men, and 57% were current smokers. The cumulative probability of ≥1 false-positive result with low-dose chest CT was 21% after 1 screening and 33% after 2 screenings. The rates with CXR were 9% and 15%, respectively. Invasive procedures were performed in 7% of participants with false-positive low-dose CT and 4% with false-positive CXR.

Conclusions: Risks for false-positive results in lung cancer screening tests are substantial after only 2 annual examinations, and further study regarding the associated economic, psychosocial, and physical burdens of these screening modalities is warranted.

Reviewer's Comments: As with all screening tests, health-care providers should discuss potential benefits and harm with patients. This study helps determine some potential risks of lung cancer screening. The ongoing National Lung Screening Study will hopefully determine any benefits of screening and help with future discussions, including whether screening can reduce mortality from lung cancer. (Reviewer-Melissa “Moe” Hagman, MD).

Keywords: Lung Cancer, Screening, CT, Chest X-Ray

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