Routine PCI After Thrombolysis?

Routine Early Angioplasty After Fibrinolysis for Acute Myocardial Infarction.

Cantor WJ, Fitchett D, et al:

N Engl J Med 2009; 360 (June 25): 2705-2718

In patients with ST-segment elevation myocardial infarction, routine percutaneous coronary intervention after lytics decreases the rate of subsequent ischemic events.

Background: Most hospitals cannot perform primary percutaneous coronary interventions (PCI) for patients presenting with ST-segment elevation myocardial infarction (STEMI). Therefore, there is still a role for thrombolysis, but the subsequent role and optimal timing of PCI remains unclear.
Objective: To compare routine PCI within 6 hours of thrombolysis with standard care (transfer for lytic failure or recurrent ischemia).
Design: Randomized, non-blinded multicenter trial.
Participants: Patients with STEMI who presented to centers without PCI capability within 12 hours of symptom onset were eligible.
Methods: All patients received tenecteplase, aspirin, and unfractionated heparin or enoxaparin. In mid-study, a recommendation for clopidogrel use was added. Patients were randomly assigned to either early PCI or standard care. In the early PCI group, patients received thrombolysis and were then immediately transferred to a PCI center to undergo coronary angiography within 6 hours. In the standard treatment arm, patients underwent repeat ECG 60 to 90 minutes after randomization and were transferred for urgent PCI if there were still significant ST elevations and chest pain or hemodynamic instability. All other patients remained in the hospital for at least 24 hours with a recommendation of coronary angiography within 2 weeks. The primary outcome was a composite of death, reinfarction, recurrent ischemia, new or worsening heart failure, or shock within 30 days.
Results: 1059 patients were entered into the study: 537 to early PCI and 522 to standard treatment. Coronary angiograms were performed in 98.5% of early PCI patients at a median of 2.8 hours after randomization. In the standard group, 88.7% underwent angiograms at a median of 32.5 hours, and roughly one third underwent urgent angiography within 12 hours of thrombolysis for ischemic events/complications. Management was similar except for higher rates of clopidogrel use in the early PCI arm. At 30 days, fewer patients in the early PCI group reached the composite end point as compared to standard therapy (11% vs 17%; P =0.004). There were no significant differences in mortality or significant bleeding. At 6 months, there were no differences seen in either death or reinfarction rates.
Conclusions: In patients with STEMI, routine PCI after lytics decreases the rate of subsequent ischemic events.
Reviewer's Comments: This study provides evidence that early angiography after thrombolysis improves outcomes. As always, composite outcomes can be a bit tricky to interpret. The outcomes studied are important ones, and a much bigger study would need to be done to investigate any of the individual components. Notably, more than one third of patients in the standard arm ended up being referred for early angiography. Therefore, it may be reasonable to give lytics, but still make plans for transfer as soon as possible. (Reviewer-Mark E. Pasanen, MD).

Keywords: ST-Segment Elevation Myocardial Infarction, Fibrinolysis, Percutaneous Coronary Intervention, Early Angioplasty

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Good News, Bad News -- New Device May Prevent Stroke in AF

Percutaneous Closure of the Left Atrial Appendage Versus Warfarin Therapy for Prevention of Stroke in Patients With Atrial Fibrillation: A Randomised Non-Inferiority Trial.

Holmes DR, Reddy VY, et al:

Lancet 2009; 374 (August 15): 534-542

A percutaneous device to occlude the left atrial appendage helps to prevent strokes, but at the cost of complications.

Background: Warfarin is the mainstay of stroke prevention in chronic atrial fibrillation (AF), but many clots are thought to originate in the left atrial appendage (LAA).
Objective: To test a percutaneous device to close the LAA for stroke prevention in AF.
Design: Randomized, active-control open-label trial.
Participants: 707 patients aged ≥18 years with a CHADS2 score of at least 1. Patients also had to be eligible for warfarin therapy.
Methods: Patients in the intervention group had their LAA closed with a WATCHMAN device. Patients with the device remained on warfarin for 45 days; they were then switched to dual-antiplatelet therapy with clopidogrel and aspirin for 6 months, and then switched to aspirin alone. These patients also received follow-up transesophageal echocardiographs at 45 days, 6 months, and 12 months. If the 45-day echocardiograph did not show satisfactory closure with the device, patients were continued on warfarin. The control group received warfarin for the duration of the study, with a target international normalized ratio between 2 and 3. The primary end point was a composite of stroke, cardiovascular or unexplained death, and systemic embolism. There was also a safety end point that was a composite of bleeding and procedure-related complications such as serious pericardial effusion, device embolization, or procedure-related stroke. Mean follow-up was 18 months.
Results: The device was successfully implanted in 88% of patients in the intervention arm. Of these, 86% were able to stop warfarin at 45 days. There were no significant differences in the composite efficacy end point between groups, but there were more hemorrhagic strokes in the warfarin group and more ischemic strokes in the intervention group. Regarding the safety end point, there were more adverse events in the intervention group, most around the time of the procedure, including 4.8% of patients who had pericardial effusion requiring drainage and 1.1% who had a procedure-related ischemic stroke. Three patients suffered from device embolization; 1 of these was successfully retrieved percutaneously, and the other 2 underwent surgery.
Reviewer's Comments: The good news is that the WATCHMAN device does appear to be effective in preventing embolic stroke from AF, at least as effective as warfarin. The bad news is that it is associated with a considerable risk for peri-procedure complications. Ironically, because of the study design randomizing patients to either a device or warfarin, the device was not tested in one population in which its use might be most appealing: those with contraindications to warfarin. The WATCHMAN device to occlude the LAA shows promise in treatment of chronic AF, but it has not yet found its niche. (Reviewer-Christopher L. Knight, MD).

Keywords: Atrial Fibrillation, Percutaneous Closure, Warfarin, Stroke Prevention

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Is Tight Control of Hypertension the Best Way to Go?

Usual Versus Tight Control of Systolic Blood Pressure in Non-Diabetic Patients With Hypertension (Cardio-Sis): An Open-Label Randomised Trial.

Verdecchia P, Staessen JA, et al:

Lancet 2009; 374 (August 15): 525-533

Tighter control by lowering systolic blood pressure levels from 140 to 130 improves clinical outcomes in patients with hypertension.

Background: Despite a great deal of data, the ideal blood pressure (BP) target when treating hypertension remains ambiguous. The literature to date has had mixed results; a number of trials have suggested better outcomes with lower average BP in high-risk patients, but few of them were intentionally designed to test treatment targets. A recent Cochrane review looked at data available at the time and concluded that there was insufficient evidence to support targets of <140/90 mm Hg.
Objective: To assess whether using a lower BP target would decrease left ventricular hypertrophy in a population that was already being treated for hypertension.
Design: Randomized open-allocation trial.
Participants: 1111 patients with a systolic BP of ≥150 and 1 additional risk factor who were on antihypertensive treatment for at least 12 weeks.
Methods: Patients were randomized to a target BP of either 140 or 130 systolic. Study physicians had many options for therapy including furosemide, ramipril, telmisartan, amlodipine, bisoprolol, and clonidine. In the tight control group, therapy was intensified if their BP was >130 at any visit. In the usual control group, BP treatment was down-titrated if their BP was <130.
Results: BP was lower in the tight control group, although only by an average of 3.8/1.5 mm Hg. The trial's primary end point was ECG left ventricular hypertrophy, which occurred in 17% of usual control patients and 11.4% of tight control patients (statistically significant). The authors also tracked a broad secondary composite end point, including death, myocardial infarction, stroke, transient ischemic attack, congestive heart failure, angina, atrial fibrillation, coronary revascularization, aortic dissection, peripheral arterial disease, and dialysis. At least 1 event in this broad composite outcome occurred in 9.4% of patients in the usual control group and in 4.8% in the tight control group (statistically significant, P =0.003). Most of the difference was in lower rates of new-onset atrial fibrillation and coronary revascularization in the tight control group.
Reviewer's Comments: There are factors in this study that are better in a study setting, but they do not replicate what we usually do in the office. The end points are also relatively limited. The study was powered specifically to look at left ventricular hypertrophy (LVH) as its primary end point, and indeed it saw a difference in LVH. The secondary end point did combine clinically relevant events, but there were many of them of variable severity. That said, this paper is helpful because it does provide additional data validating aggressive control of BP in patients at moderate risk, a stance that makes some intuitive sense but on which data have been mixed. (Reviewer-Christopher L. Knight, MD).

Keywords: Hypertension, Systolic, Usual vs Tight Control

Print Tag: Refer to original journal article

New Persistent Pain Management Guidelines for the Elderly

Pharmacological Management of Persistent Pain in Older Persons.

American Geriatrics Society Panel:

J Am Geriatr Soc 2009; 57 (August): 1331-1346

If acetaminophen fails to adequately manage persistent pain, opiates are a more appropriate second-line agent than NSAIDs in older persons.

Objective: To update Clinical Practice Guidelines on managing persistent pain in older persons.
Methods: Expert review of evidence and panel consensus. Guidelines focused on persons aged ≥75 years with chronic illnesses and/or frailty. **Recommendations:** Acetaminophen should be first-line therapy for pain in older adults. Doses can be titrated up to 1000 mg 4 times daily, not to exceed 4 g total in 24 hours from all sources. NSAIDs have been implicated in up to 25% of hospitalizations due to adverse drug reactions in older adults, and their use should be avoided in managing persistent pain in the elderly. Topical NSAIDs such as diclofenac or salicylate derivatives may have some efficacy for managing localized pain. All older patients with moderate to severe pain or pain-related functional impairment should be considered for opioid therapy. Opioids should be initiated using low doses of shorter-acting opiates. Toxic metabolites of morphine may limit usefulness of long-acting morphine agents in persons with renal insufficiency or when high-dose therapy is required. Adjuvant drugs such as gabapentin, pregabalin, duloxetine, or venlafaxine should be considered for neuropathic pain. There is a small role for muscle relaxants in managing persistent skeletal muscle pain. If muscle spasm is suspected to be a root cause of pain, drugs with known effects on muscle spasm such as Lioresal (baclofen) can be considered.
Reviewer's Comments: The approach to pain management in older persons differs from that for younger people. Pain assessment in the elderly is often complicated by underreporting and/or difficulties in recognizing pain with cognitive impairment. The elderly are at higher risk for experiencing adverse drug effects owing to concomitant disease, pharmacological changes with aging, and presence of polypharmacy. Despite these challenges, pain can and must be effectively managed in this patient population. Goals of pharmacologic management are to reduce pain to a level that allows adequate function and an acceptable quality of life. While there may be a role for short-term use of NSAIDs, I endorse the panel's recommendation that NSAIDs be considered only rarely and with extreme caution in highly selected individuals with persistent pain. When using opioids, clinicians should be aware that older patients have a greater analgesic sensitivity to opiates than do younger patients, so initial doses should be low, with dose increases carefully carried out as needed. Most adverse effects of opioids decrease with long-term use with the exception of constipation, which must be addressed with appropriate bowel regimens. Although older age is associated with a much lower risk for opioid misuse or abuse, clinicians should remain vigilant about this possibility. The authors stress that these recommendations are intended as a guide rather than as dogma and are not a replacement for critical thinking, sound judgment, and clinical experience. (Reviewer-Jeff Wallace, MD, MPH).

Keywords: Persistent Pain, Older Adults, Pharmacologic Treatment

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Pain Is Common, May Impair Function in Older Adults

Comparing Pain Severity Versus Pain Location in the MOBILIZE Boston Study: Chronic Pain and Lower Extremity Function.

Eggermont LHP, Bean JF, et al:

J Gerontol A Biol Sci Med Sci 2009; 64A (July): 763-770

Many older persons have multisite pain, a symptom that is associated with poorer lower-extremity function.

Background: Persistent pain is felt to be a major cause of disability in older adults.
Objective: To explore the association between 2 measures of chronic pain (number of pain sites and overall pain severity) and lower-extremity (LE) function in older adults.
Design: Cross-sectional study.
Participants/Methods: 600 older adults in the greater Boston area participating in a population-based study of risk factors for falls were queried about persistent pain symptoms and underwent performance-based tests of LE function. When present, pain was categorized by number of sites and by a summary measure of overall pain severity. LE function tests included gait speed, balance, and chair stands. These performance-based tests have been shown to predict adverse events in older persons, such as disability, falls, institutionalization, and death.
Results: Average age of subjects was 78 years, and two thirds were women. Two thirds of subjects reported pain at ≥1 site, and 40% had multisite or widespread pain symptoms. Both multisite/widespread pain and the highest quartile of overall pain severity were associated with LE functional abilities. In multivariate analyses that included adjustments for age, weight, and comorbid conditions, multisite/widespread pain was the variable most significantly associated with diminished LE function. Only pain that was rated in the highest quartile of pain severity was associated with reduced LE functional performance. When specific joint pain sites were evaluated, only knee pain was independently associated with lower functional ability scores.
Conclusions: Pain at multiple sites was more strongly associated with LE function than overall pain severity or pain at specific locations.
Reviewer's Comments: I included this article among my reviews this month to help highlight the importance of optimizing pain management in older adults. Pain can adversely affect functional abilities, which in turn are associated with undesirable events such as falls or institutionalization. This study demonstrates the association between pain, especially when present at multiple sites or when rated in the most severe quartile, and diminished LE functional abilities. The cross-sectional design of this study limits conclusions about the causal association between pain and reduced functional status. Furthermore, one cannot conclude from this study that treating and reducing pain will translate into improved functional abilities and better clinical outcomes. The fact that only more severe pain was associated with reduced LE function raises the possibility that even modest pain relief could lead to significant changes in function, especially in persons with moderate to severe pain. At a minimum, treating pain can improve quality of life, and future studies will hopefully demonstrate that improved pain management can also favorably impact functional status and improve health outcomes. (Reviewer-Jeff Wallace, MD, MPH).

Keywords: Chronic Pain, Lower-Extremity Function, Older Adults

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Feeding Tubes, Nursing Home, Advanced Dementia -- Not a Good Combination

Natural History of Feeding-Tube Use in Nursing Home Residents With Advanced Dementia.

Kuo S, Rhodes RL, et al:

J Am Med Dir Assoc 2009; 10 (May): 264-270

The majority of nursing home patients with advanced dementia who receive new feeding tubes are dead within 1 year.

Background: Despite a growing body of evidence questioning the clinical benefit of tube feeding in older patients with advanced dementia, this intervention continues to be frequently used.
Objective: To determine national percutaneous endoscopic gastrostomy (PEG) feeding-tube insertion rates, and to explore the natural history after feeding-tube placement in nursing home residents with advanced dementia.
Design: Secondary analysis of national Minimum Data Set and Medicare Claims Files from 2000 to 2002.
Participants/Methods: Nursing home residents aged ≥66 years with advanced dementia were followed for 1 year to determine PEG-tube incidence rates and for 1 year after PEG-tube insertions for complications and other health-related outcomes.
Results: Average age of subjects was 84 years, and most were very dependent in their activities of daily living. The national incidence rate for feeding-tube insertion was 53.6 per 1000 older nursing home patients with advanced dementia. Rates varied widely by state from a low of 2.1/1000 patients in Utah to >100.0/1000 in Mississippi and Alabama. Persons who received PEG tubes were more likely to be non-white, male, and to lack advance directives. Of all feeding tubes, 68% were inserted during an acute care hospitalization. The common diagnosis associated with feeding-tube insertions in the hospital was aspiration pneumonia (17%). The 1-year mortality rate among residents who had a feeding tube inserted was 64%. Median survival among those who died was 56 days. Nearly 20% of residents required subsequent replacement of their feeding tubes within 1 year, with >5% requiring at least 2 replacements.
Conclusions: Feeding-tube insertions are associated with poor survival in nursing home residents with advanced dementia, and there likely is a need for improved decision-making around feeding tubes in such patients. Because most PEG tubes are inserted during acute hospital care stays, the authors suggested that hospitals are the most common final locus of decision-making regarding feeding tubes, and that interventions to reduce the variation in feeding-tube insertions may best be targeted in the acute care setting.
Reviewer's Comments: I am often requested by dieticians or speech therapists to have discussions with families about whether feeding tube should be considered for their loved ones with advanced dementia who can no longer maintain adequate nutrition or hydration on their own. This study indicates that the prognosis is grim even when PEG tubes are inserted, and that there is a fair chance patients will suffer complications such as the need to return to the hospital for reinsertion of PEG tubes. These data add to a mounting body of evidence that feeding-tube use in patients with advanced dementia is often associated with morbidity, with little evidence of benefit on nutritional status or clinical outcomes. (Reviewer-Jeff Wallace, MD, MPH).

Keywords: Feeding Tubes, Nursing Home Residents, Advanced Dementia

Print Tag: Refer to original journal article

Specialized Nutritional Supplements May Aid Healing of Pressure Ulcers

Disease-Specific, Versus Standard, Nutritional Support for the Treatment of Pressure Ulcers in Institutionalized Older Adults: A Randomized Controlled Trial.

Cereda E, Gini A, et al:

J Am Geriatr Soc 2009; 57 (August): 1395-1402

A nutritional supplement enriched with protein, arginine, zinc, and vitamin C may accelerate pressure ulcer healing.

Background: Although nutritional health may be an important component of managing pressure ulcers (PUs), evidence demonstrating benefits of nutritional interventions on ulcer healing is not robust.
Objective: To test the effect of a specific nutritional supplement on PU healing relative to standard dietary supplementation.
Design: Randomized controlled trial.
Participants/Methods: Persons aged ≥65 years in long-term care facilities in Italy, without diabetes, peripheral vascular disease, or neoplastic disorders, were screened for PUs. Twenty-eight patients with stage 2 to 4 pressure ulcers present for <1 month were enrolled and were followed for 12 weeks for the primary end point of PU healing as evaluated by the Pressure Ulcer Scale for Healing (PUSH) tool and ulcer area measurements.
Interventions: 15 control subjects received standard nutrition using a hospital diet or standard enteral formulas; 13 subjects received standard diets plus a supplement enriched with protein, arginine, zinc, and vitamin C.
Results: Although baseline demographics, nutritional status, and ulcer severity measures were not statistically significantly different, treatment group patients weighed less (54 vs 64 kg) and had a lower average body mass index (21 vs 23 kg/m2) than did controls. Nine patients in each group were tube fed. The treatment protocol resulted in higher intakes of protein (1.5 vs 1.2 g/kg per day), arginine, zinc, and vitamin C. At 12 weeks, both groups had significant improvements in PU size. Persons in the enriched supplement group showed significantly (P <0.05) faster rates of healing per changes in PUSH scores (-6.1 vs -3.3), ulcer size (-1.45 cm2 vs -0.84 cm2), and percent reduction in ulcer size (72% vs 45%).
Conclusions: PU healing rates were faster among persons receiving an enriched nutritional formula. Disease-specific nutritional support should be considered in elderly institutionalized persons with PUs, although larger randomized controlled trials are needed to confirm these preliminary findings.
Reviewer's Comments: This study was well designed and conducted but still has several methodologic issues that limit conclusions about the utility of the study nutritional supplement. First, the small subject numbers greatly limited comparisons of baseline measures between control and treatment groups. For instance, treatment group subjects weighed 20 pounds less than controls, but this difference did not reach statistical significance. No adjustments were made for this or other potential confounders. It is possible that treatment subjects were in worse baseline nutritional health and had more to gain from supplementation than did controls. Also, the study population was unique in that >60% of persons were being tube fed. No patients with diabetes or peripheral vascular disease, common problems in patients with PUs, were included in the study. This greatly limits extrapolating findings to other populations of older adults. The results are intriguing but, as the authors stated, further high-quality studies are needed to confirm these preliminary results. (Reviewer-Jeff Wallace, MD, MPH).

Keywords: Nutritional Support, Pressure Ulcers, Older Adults

Print Tag: Refer to original journal article

Don't Overlook Bruises on Older Adults as Sign of Possible Elder Abuse

Bruising as a Marker of Physical Elder Abuse.

Wiglesworth A, Austin R, et al:

J Am Geriatr Soc 2009; 57 (July): 1191-1196

Older adults with larger bruises or bruises on the face, lateral arm, or posterior torso may be victims of elder abuse and should be asked about the cause of their bruises.

Background: Although some clinicians and Adult Protective Services (APS) workers have learned to be suspicious of unusual bruising, little is known about the nature of bruising associated with physical elder abuse.
Objectives: To determine the percentage of elder abuse victims with bruises; to document the location, size, and victim-stated causes of bruises; and to explore differences in bruises among older adults who have and have not been physically abused.
Participants/Methods: Persons aged ≥65 years referred to APS because of alleged elder abuse were contacted to participate in this study. A prior 2005 study of accidental bruising in older persons residing in institutionalized settings without elder abuse provided "control" data for comparison.
Results: <20% of 407 potentially eligible, alleged physical abuse victims were enrolled in the study. Mean age of abuse victims was 77 years, 70% were women, and most were Caucasian. Bruises were found on 72% of subjects. Compared to persons with accidental bruises, physical abuse victims were more likely to have large (>5 cm) bruises (7.3% vs 56.2%, respectively) and to know the cause of at least 1 bruise (28.6% vs 91.0%, respectively). Victims of physical abuse more often had bruises on the face, neck, or torso than did persons with accidental bruises (40% vs 13%, respectively) and bruises on the right lateral arm (25% vs 7%, respectively).
Conclusions: Bruises that occur as a result of elder abuse are often large and more likely to be present on the face, posterior torso, and right lateral arm relative to persons with accidental bruises. Older adults with suspicious bruises should be asked about their cause to better detect possible physical abuse.
Reviewer's Comments: This study had to be enormously difficult to carry out, and it is therefore not surprising that it is the first to address characteristics of bruising associated with elder abuse. My main concern about the validity of these findings is that study subjects were community-dwelling elderly, while controls resided in assisted living and nursing home facilities. It is conceivable that accidental bruise patterns might differ between institutionalized and community-dwelling elderly. It is somewhat reassuring that these findings (ie, bruises associated with elder mistreatment are large and often occur on the face and posterior trunk) are consistent with those in the literature on bruising associated with child abuse. The finding of increased bruising on the right lateral arm has not previously been noted in the pediatric literature and may be a chance finding. Despite these potential study limitations, I agree with the authors' suggestion that physicians who see older adults with large bruises or bruises in suspicious locations (face, neck, posterior torso) should ask about their cause. Clinicians should act on such suspicions with referral to APS. (Reviewer-Jeff Wallace, MD, MPH).

Keywords: Elder Abuse, Bruising, Marker

Print Tag: Refer to original journal article

People Who Receive CPR Have Better Chance of Leaving Hospital Alive

Epidemiologic Study of In-Hospital Cardiopulmonary Resuscitation in the Elderly.

Ehlenbach WJ, Barnato AE, et al:

N Engl J Med 2009; 361 (July 2): 22-31

Of patients aged >65 years who are resuscitated in the hospital, about 18% will survive to discharge, and 8% will discharge to home.

Background: To make informed choices about resuscitation, both physicians and patients need accurate, current information about the likelihood of survival.
Objective: To describe the incidence and outcomes of in-hospital cardiopulmonary resuscitation (CPR), as well as patient and hospital characteristics associated with survival.
Design: Retrospective epidemiologic review.
Methods: The authors reviewed all Medicare hospital claims data for traditional fee-for-service patients aged ≥65 years during the years 1992 to 2005. They identified 433,985 patients who received in-hospital CPR during that time. They collected demographic information for each patient and assigned a score for the burden of chronic illness using the Deyo-Charlson comorbidity index. Possible scores on this index range from 0 to 33, with higher scores meaning more comorbidities.
Results: Overall, 18.3% of patients receiving CPR survived to hospital discharge. There was no increase in the rate of survival from 1992 through 2005. The likelihood of survival to discharge decreased with increasing age, from 22.2% in 65- to 69-year-olds, to 12.0% in aged >90 years. Women were more likely to survive to discharge (19.2%) than were men (17.5%). Patients with a higher burden of chronic illness had a lower likelihood of survival: 16.1% for those with scores of ≥3 versus 19.0%, on average, for those with scores of 0, 1, or 2. Not surprisingly, admission from a skilled nursing facility was associated with a much lower likelihood of survival (11.5%). Black and other non-white patients were significantly less likely to survive to discharge (14.3% and 15.9%, respectively) than were white patients (19.2%). Patients admitted with congestive heart failure or myocardial infarction were slightly but significantly more likely to survive, while those admitted with stroke were no more or less likely to survive CPR than average. Over time, the number of survivors discharged to home rather than a nursing facility or other hospital fell from about 60% to <40%, although this may reflect earlier discharge rather than more debility.
Conclusions: Survival to hospital discharge following CPR has not improved in recent years, and remains around 18%. Older age and more chronic illness were associated with lower survival, as were male sex and non-white race.
Reviewer's Comments: This study gives us the "big picture" on survival following in-hospital CPR: it hasn't improved, but the average patient who receives CPR has an 18% chance of leaving the hospital alive. Accurate current information on survival in patients with more specific diseases, such as advanced cancer or chronic renal failure, would be welcome. (Reviewer-Karen A. McDonough, MD).

Keywords: Cardiopulmonary Resuscitation, In-Hospital, Elderly, Survival Rate

Print Tag: Refer to original journal article

Man's Best Friend?

Nonfatal Fall-Related Injuries Associated With Dogs and Cats -- United States, 2001-2006.

Staff Writers:

MMWR 2009; 58 (March 27): 277-281

Dogs and cats cause an increased risk of falls, with fractures occuring from the falls most commonly in patients aged ≥75 years.

Background: Falls are the leading cause of nonfatal injuries in the United States. Falls are especially common in the elderly, occuring in 30% to 40% of people aged >65 years annually. Falls are also very common in children, leading to >2 million emergency department visits annually. Environmental factors play a significant role in fall risk.
Objective: To assess the incidence of fall-related injuries associated with dogs and cats.
Methods: The Centers for Disease Control and Prevention analyzed data from the National Electronic Injury Surveillance System All Injury Program over a 5-year period (2001-2006). The program collects data on visits for all injuries treated in emergency departments from a sample of 66 hospitals in the United States.
Results: An estimated average of 86,629 fall injuries occurred annually in association with dogs and cats. The average annual injury rate was 29.7 per 100,000 population. Most injuries (88%) were associated with dogs, with women more likely to be injured than men. Although injuries were most frequent in younger individuals, the rate of fractures was highest in patients aged ≥75 years. Tripping over cats was the most common cause of cat-related falls (66.4%), as well as dog-related falls (31.3%). Being pushed or pulled by a dog while walking them was an important cause of falls (21.2%). Tripping over a pet-related item accounted for 8.8% of falls.
Conclusions: Pet ownership is an important risk for falls.
Reviewer's Comments: Anyone who owns a pet will not be surprised by the findings of this study. There are several studies that show a health benefit for pet owners, so elimination of pets may decrease fall risk but may not improve health overall. Common sense interventions may decrease the risk of falls associated with pet ownership such as obedience training for dogs to minimize behaviors associated with falls (eg, pushing or pulling) and keeping pet play toys limited to a certain area. (Reviewer-Douglas S. Paauw, MD).

Keywords: Falls, Injuries, Dogs, Cats

Print Tag: Refer to original journal article

Combined Tx Useful for Menstrual Migraine

Combination Treatment for Menstrual Migraine and Dysmenorrhea Using Sumatriptan-Naproxen: Two Randomized Controlled Trials.

Mannix LK, Martin VT, et al:

Obstet Gynecol 2009; 114 (July): 106-113

Sumatriptan-naproxen is effective in the treatment of menstrual migraine when used early after symptom onset.

Background: Migraine headaches occuring regularly with menses occur in more than half the women who have migraines, and 14% have their migraines exclusively during their menstrual periods. These headaches may be more severe and persistent than migraine headaches not associated with menses.
Objective: To evaluate the efficacy of combined sumatriptan-naproxen during the mild pain phase of a single menstrual migraine attack associated with dysmenorrhea.
Methods: 2 identically designed, multicenter, randomized, double-blind placebo-controlled studies of treatment of menstrual migraine with sumatriptan-naproxen were conducted using 30 sites for study 1 and 34 sites for study 2. Eligibility criteria were women aged ≥18 years who had at least a 6-month history of migraine along with a history of at least 6 migraine headaches per month for the past 3 months, and with attacks occuring during menstrual periods during at least 2 of the past 3 months. Patients treated their migraine attack within 1 hour of onset of symptoms with sumatriptan 85 mg and naproxen as a single fixed-dose tablet or placebo. The primary end point was being pain free at 2 hours.
Results: In study 1, a total of 311 patients were enrolled, and 310 patients were enrolled in study 2. The sumatriptan-naproxen combination was superior to placebo in both studies, with a 42% versus 23% 2-hour pain-free response rate in study 1 and 52% versus 22% pain-free response rate in study 2 (P <0.001 for both studies). Pain-free response rates from 2 to 24 hours were less, with a rate of 29% versus 18% (P =0.02) in study 1 and 38% versus 10% (P <0.001) in study 2.
Conclusions: Sumatriptan-naproxen was an effective treatment for menstrual migraine.
Reviewer's Comments: This study shows that sumatriptan-naproxen is effective in the treatment of menstrual migraine. This isn't a surprise as triptans alone have been shown to be effective in the treatment of menstrual migraine. The weakness of this study is that there is no arm comparing sumatriptan versus sumatriptan-naproxen. It isn't clear that the naproxen adds anything to sumatriptan for migraine treatment. A large study published in *JAMA* in 2007 did look at the combination compared to either component alone and found the combination was superior to both sumatriptan and naproxen by themselves. (Reviewer-Douglas S. Paauw, MD).

Keywords: Menstrual Migraine, Dysmenorrhea, Sumatriptan, Naproxen

Print Tag: Refer to original journal article

Harm From Combination Hormone Tx: This Time It's Lung Cancer

Lung Cancer Mortality Higher in Women Who Used Combination Hormone Therapy.

Hampton T:

JAMA 2009; 302 (August 12): 615-616

The Women's Health Initiative now adds increased lung cancer mortality to the list of risks posed by combination estrogen-progestin after menopause.

Background: Retrospective studies have not consistently demonstrated any effect of menopausal hormone therapy (HT) on mortality from lung cancer. The Women's Health Initiative (WHI), a prospective randomized trial that, in 2002, showed a higher risk of breast cancer but lower risk of colon cancer in postmenopausal women on combination HT, subsequently reported higher risks from combination HT of both ovarian cancer and advanced colon cancer.

Objective/Design: To report data presented at the 45th Annual Meeting of the American Society of Clinical Oncology. Dr Rowan Chlebowski and the WHI investigators studied the incidence and mortality from non-small-cell lung cancer after 5.6 years of combination HT and 2.4 years of additional follow-up, for a total of 8.0 years.

Results: Incidence rates of lung cancer were not different between women assigned to combination HT and those assigned placebo, but the mortality rate from lung cancer over the 8 years was 3.4% in smokers on HT versus 2.3% among smokers on placebo. Researchers estimated that 1 in 100 current smokers assigned to HT died avoidably over the 8 years of this study.

Conclusions: Combination HT increases the mortality rate, but not the incidence rate, of non-small-cell lung cancer in postmenopausal women. Women who smoke should hear about this increased risk if considering use of combination HT.

Reviewer's Comments: This article reports the first data from any prospective randomized trial on HT's effect on lung cancer, with startling findings: 4 per 1000 women per year among current smokers assigned to combination HT in the WHI died of non-small-cell lung cancer (approximately 50% higher than with placebo). The study is not yet published, but given the well-established track record of the WHI and this lead author, Dr Rowan Chlebowski, expect the full scientific article in print before long. (Reviewer-Eliza L. Sutton, MD).

Keywords: Hormone Therapy, Menopause, Lung Cancer

Print Tag: Refer to original journal article

Does Cutting Back on Sleep Cause Type 2 Diabetes?

Exposure to Recurrent Sleep Restriction in the Setting of High Caloric Intake and Physical Inactivity Results in Increased Insulin Resistance and Reduced Glucose Tolerance.

Nedeltcheva AV, Kessler L, et al:

J Clin Endocrinol Metab 2009; 94 (September): 3242-3250

Allowing ≥7 hours of sleep each night improves glucose tolerance and insulin sensitivity, reduces catecholamine levels, and leads to less snacking compared with cutting sleep to 5 hours each night.

Background: Sleep duration now averages approximately 6 hours each night during the workweek in the United States; obesity and diabetes rates keep rising. Sleep deprivation and type 2 diabetes are linked in epidemiologic studies. Short-term experimental sleep restriction to 4 hours impairs glucose tolerance, but ongoing sleep restriction has not been studied.

Objective: To characterize effects of reducing sleep to 5 to 6 hours/night for 2 weeks on glucose metabolism in healthy overweight sedentary adults.

Design/Participants: Randomized crossover study of 11 sedentary overweight volunteers (mean age, 39 years; body mass index, 26.5 kg/m2; average sleep, 7.6 hours/night) during two 14-day inpatient blocks with food, but not exercise, freely available.

Methods: The intervention was restricting maximum sleep to 5.5 hours/night or 8.5 hours/night. After 2 weeks, each subject underwent oral then IV glucose tolerance testing, with blood sampled frequently over 24 hours for insulin and counterregulatory hormone levels.

Results: Subjects slept 2 hours/night less during sleep restriction (mean, 5.2 hours vs 7.2 hours). Nutrient intake, total caloric intake, and weight gain (mean, 2 kg) did not differ between sessions, but snacking was more frequent during sleep restriction. After sleep curtailment, post-load glucose was higher at 2 hours (144 vs 132 mg/dL) and 3 hours, insulin sensitivity was reduced, epinephrine levels were persistently higher, and norepinephrine levels were higher overnight. Cortisol and growth hormone levels did not differ.

Conclusions: Limiting sleep, the current cultural norm, impairs glucose tolerance in overweight sedentary adults.

Reviewer's Comments: Americans readily curtail sleep, an essential but little-understood physiologic state, in favor of other pastimes. Just 2 hours/night of sleep loss impairs carbohydrate metabolism, causes sympathetic activation, and increases snacking. In the sedentary population and environment studied here, ad lib access to food resulted in 2 kg of weight gain every 2 weeks (500 excess kcal ingested each day). Adequate sleep, regular exercise, and conscious self-monitoring of caloric balance may all be necessary to prevent type 2 diabetes. (Reviewer-Eliza L. Sutton, MD).

Keywords: Sleep Deprivation, Glucose Intolerance, High Caloric Intake, Physical Inactivity

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Once-Daily Liraglutide Better Tolerated for Type 2 Diabetes

Liraglutide Once a Day Versus Exenatide Twice a Day for Type 2 Diabetes: A 26-Week Randomised, Parallel-Group, Multinational, Open-Label Trial (LEAD-6).

Buse JB, Rosenstock J, et al:

Lancet 2009; 374 (July 4): 39-47

Liraglutide, a once-daily glucagon-like peptide-1 inhibitor, is effective and well tolerated in type 2 diabetes, with a need for continued surveillance for adverse effects.

Background: The first glucagon-like peptide-1 (GLP-1) analog, exenatide (Byetta®), has shown benefit in diabetes with both improved glycemic control and weight loss. However, it had trouble with side effects and twice-daily subcutaneous dosing.
Objective: To compare a new, once-daily injectable GLP-1 analog, liraglutide (Victoza®), to exenatide in patients with type 2 diabetes.
Design: Randomized open-label active-control trial.
Participants: 464 patients between the ages of 18 and 80 years with type 2 diabetes, a hemoglobin A_{1c} value between 7% and 11%, and a body mass index of <45 were eligible if they had been treated with metformin, sulfonylurea, or both for at least 3 months at study entry. Patients who had previously been treated with insulin or GLP-1 analogs were excluded, as were patients with impaired liver function, clinically significant cardiovascular disease, nephropathy, retinopathy, or cancer.
Interventions: Patients were randomized to 1 of 2 open-label arms: exenatide 10 µg twice daily or liraglutide 1.8 mg once daily. Oral antidiabetic drugs were continued and were only reduced in the case of hypoglycemia.
Results: About 15% of each group withdrew from the study, usually because of adverse events. Hemoglobin A_{1c} reduction with liraglutide was 1.16%, compared to exenatide's 0.87%. Patients on liraglutide also showed slightly greater reductions in fasting glucose and weight, while patients on exenatide showed greater reductions in postprandial glucose. The liraglutide group had lower overall rates of adverse events, but more serious and severe adverse events than the exenatide group. Notably, nausea seemed to diminish after the initial run-in period for more patients on liraglutide than exenatide.
Conclusions: Liraglutide once a day provided significantly greater improvements in glycemic control than did exenatide twice a day, and was generally better tolerated. The results suggest that liraglutide might be a treatment option for type 2 diabetes, especially when weight loss and risk of hypoglycemia are major considerations.
Reviewer's Comments: This trial is unusual and commendable in that it compares a new drug with an older drug in the same class. Because of this, it's easier to say that liraglutide does possess measurable advantages over exenatide. The trial is limited by the fact that it was open-label rather than blinded, so results should be approached with caution. However, to the extent that we believe the results, liraglutide shows slightly better glycemic control, overall better tolerability, and has the advantage of once-daily dosing. The issue of serious adverse events, particularly pancreatitis, does bear continued watching. However, even a skeptic like myself is forced to admit that, at least in this manufacturer-sponsored study, liraglutide appears to be more than just a "me-too" drug. Hopefully we'll continue to see more comparative research like this in the future. As for what we'll prescribe: a once-weekly formulation of exenatide is also in the pipeline, so who knows? (Reviewer-Christopher L. Knight, MD).

Keywords: Liraglutide, Exenatide

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Denosumab Reduces Fracture Rates in Postmenopausal Women

Denosumab for Prevention of Fractures in Postmenopausal Women With Osteoporosis.

Cummings SR, San Martin J, et al:

N Engl J Med 2009; 361 (August 20): 756-765

Denosumab is given as a twice-yearly subcutaneous injection, is well tolerated, and significantly reduces the risk of vertebral and nonvertebral osteoporotic fractures.

Background: Denosumab, a fully human monoclonal antibody that inhibits osteoclast formation and activity, reduces bone loss and increases bone density. As a monoclonal antibody, it could increase risk of infections or cancer.
Objective: To determine the effect of denosumab on the rate of new vertebral and nonvertebral fractures in postmenopausal women with osteoporosis, and to evaluate for treatment-related adverse effects.
Design/Participants: Randomized controlled trial of denosumab in women with T-score -2.5 to -4.0 at spine or hip who met a number of exclusion criteria including no prior bisphosphonates, and who consented to forego available osteoporosis treatments.
Methods: Denosumab 60 mg or placebo was given subcutaneously every 6 months for 36 months. Annual lateral spine radiographs were evaluated for radiographic vertebral fractures, and information was gathered on new clinically apparent osteoporotic fractures and potential adverse effects.
Results: On placebo, 7.0% of women developed new vertebral fractures by radiography, 2.6% had new vertebral fractures diagnosed clinically, and 1.6% had multiple new vertebral fractures. Each of these rates was reduced by two thirds in women on denosumab (*P* <0.001). On placebo, 8% of women had nonvertebral osteoporotic fractures; this rate was 20% lower in women on denosumab (P =0.01). On placebo, 1.2% of women sustained hip fractures; this rate was 40%lower in women on denosumab (P =0.04). There were no cases of hypocalcemia or jaw osteonecrosis, and no difference in the rates of infection overall or of cancer. The following adverse events occurred more frequently on denosumab: eczema (3.0% vs 1.7%), flatulence (2.2% vs 1.4%), and cellulitis (0.3% vs <0.1%).
Conclusions: Denosumab 60 mg administered subcutaneously every 6 months reduces the risk of osteoporotic fractures in postmenopausal women without significant adverse effects.
Reviewer's Comments: Each of the several medications currently available for osteoporosis has significant limitations. Denosumab, under consideration by the FDA, is a novel treatment that may prove a useful addition to this armamentarium. Questions remain: the medication's cost, the ideal duration of therapy, the durability of benefit, and its safety profile once in more widespread use. (Reviewer-Eliza L. Sutton, MD).

Keywords: Osteoporosis, Denosumab, Fracture Prevention, Postmenopausal Women

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In Bariatric Surgery, Consider Short-Term Safety, Long-Term Effects

Perioperative Safety in the Longitudinal Assessment of Bariatric Surgery.

Longitudinal Assessment of Bariatric Surgery Consortium:

N Engl J Med 2009; 361 (July 30): 445-454

The risk of death and complications following bariatric surgery is increased by a history of venous thromboembolism and sleep apnea, but not by other coexisting conditions.

Background: In extremely obese patients, bariatric surgery may reverse diabetes and reduce both cardiovascular disease and mortality.
Objective: To report the incidence of adverse outcomes of bariatric surgery and associated patient factors.
Design: Prospective observational study.
Participants: 4776 adult patients who had bariatric surgery performed by 1 of 33 participating surgeons at multiple hospitals between March 2005 and December 2007.
Methods: Standard data were collected before, during, and after the surgery. Coexisting illnesses were as reported by the patient. Primary outcome was a composite of events measured at 30 days: death; venous thromboembolism (VTE); need for surgical, percutaneous, or endoscopic intervention; and failure to be discharged.
Results: Patients' mean age was 45 years, and mean BMI was 47. Overall, 82% had at least 1 coexisting condition: hypertension (55%), sleep apnea (49%), diabetes (32%), and asthma (23%) were the most common. Known cardiac disease was relatively rare; only 4.4% reported coronary artery disease and 2% had congestive heart failure. Limited functional status, defined as an inability to walk 200 feet, was present in 1.8% of patients. A total of 25% of patients had laparoscopic gastric banding, 59% had laparoscopic gastric bypass, and 9% had open gastric bypass. Open gastric bypass patients had the highest BMI and burden of coexisting illness, and laparoscopic gastric banding patients had the lowest. The 30-day mortality was 0.3%, ranging from 0% with gastric banding to 0.2% with laparoscopic gastric bypass to 2.1% with open gastric bypass. The composite end point occurred in 4.1% overall: 1.0% with gastric banding, 4.8% with laparoscopic gastric bypass, and 7.8% with open gastric bypass. Two coexisting conditions, sleep apnea and a history of VTE, and limited functional status were associated with higher risk, as was a BMI >53. Other coexisting conditions, such as age, sex, and race were not associated with a significant change in risk.
Conclusions: The overall risk of mortality and the composite end point following bariatric surgery was low, but varied according to patient and surgical procedure.
Reviewer's Comments: Although mortality and complications are less frequent with laparoscopic gastric banding, patients who had this procedure were, on average, lighter and healthier. The weight loss seen after gastric banding is significantly less than that seen with gastric bypass, and the impact on diabetes may be less, so gastric bypass is still the recommended procedure for many patients. Patients in this cohort were relatively young and had a low rate of pre-existing cardiac disease. (Reviewer-Karen A. McDonough, MD).

Keywords: Obesity, Weight Loss Surgery, Adverse Outcomes

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Vertebroplasty Is Attractive Option for Back Pain, but Not Very Effective

A Randomized Trial of Vertebroplasty for Osteoporotic Spinal Fractures.

Kallmes DF, Comstock BA, et al:

N Engl J Med 2009; 361 (August 6): 569-579

Vertebroplasty was no better than a sham procedure in patients with painful osteoporotic vertebral fractures.

Background: Management of acute osteoporotic vertebral fractures is difficult. Given the degree of pain and limited treatment options, patients are frequently referred for vertebroplasty. However, the benefits and risks of this procedure have not been well-documented in randomized trials.
Objective: To determine whether vertebroplasty reduces pain and back pain-related disability as compared to a sham procedure.
Design: Randomized controlled trial.
Participants: Patients aged ≥50 years with painful vertebral fractures (pain level at least 3 of 10) that had been present <1 year were eligible. Exclusion criteria included active infection, concern for neoplasm, and concomitant hip fracture.
Methods: At baseline, patients completed pain and disability surveys. All patients were brought to the fluoroscopy suite, underwent conscious sedation, and had local anesthetic administered. Patients were then randomized to either full vertebroplasty or a control procedure. For vertebroplasty, a needle was passed into the affected vertebra and medical cement was then infused. For the control group, no further intervention was performed (but similar other processes, such as opening the cement, were followed). Follow-up was done at 30 days, at which time measures of pain and disability were obtained. After 1 month, patients were allowed to cross over to the other study group. **Results**: 131 patients were enrolled in the study: 68 to vertebroplasty and 63 to the control-simulated procedure. Mean age was approximately 74 years, mean duration of pain was 16 to 20 weeks, and average pain score over the prior 24 hours before the procedure was approximately 7 of 10. Within 3 days, both groups showed significant improvement with pain scores down to approximately 4 of 10 in both groups. This degree of pain relief was sustained out to 30 days. There were not significant differences in improvement between the 2 groups. Disability scores also improved to similar degrees in both groups, once again without significant differences. Interestingly, at 3 months, crossover rates were much higher in patients in the control group (43% vs 12%; P >0.001).
Conclusions: Vertebroplasty was not associated with better pain improvement or less back pain-related disability as compared to a simulated procedure.
Reviewer's Comments: Given the lack of options in assisting patients with painful osteoporotic spine fractures, vertebroplasty has become an attractive option. However, here we are confronted with data that show that sham procedures work as well as the real thing. Clearly, patients feel better after getting a procedure. But, since the sham procedure is not an option for patients, should we continue to refer for vertebroplasty? We know they'll feel better, but realize it's mainly a placebo effect. Time will tell how this information is used in practice. (Reviewer-Mark E. Pasanen, MD).

Keywords: Vertebral Fractures, Vertebroplasty, Osteoporosis, Pain Reduction, Disability

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Visualize Colon Without Sedation, but Be Wary of Sensitivity

Capsule Endoscopy Versus Colonoscopy for the Detection of Polyps and Cancer.

Van Gossum A, Navas MM, et al:

N Engl J Med 2009; 361 (July 16): 264-270

Capsule endoscopy can be used to visualize the colon, but its sensitivity in identifying colonic lesions is approximately 65% to 75% in high-risk patients.

Background: Colonoscopy is the "gold-standard" for colorectal screening. However, many patients are unwilling to undergo this testing. Therefore, there continues to be interest in other screening modalities. Capsule endoscopy uses an ingestible capsule with video cameras at each end. It has been used for small bowel visualization, and has now been modified to allow imaging of the colon.
Objective: To determine how capsule endoscopy compares to colonoscopy in the detection of colorectal polyps and cancers.
Design: Prospective multicenter study.
Participants: Patients were eligible if they were either known or suspected to have colonic disease and had been scheduled for colonoscopy. Those with known disease included patients with a history of adenomatous polyps or cancer who had not had colonic evaluation for at least 3 years, patients with abnormal radiographic findings, and patients with ulcerative colitis. Those with suspected disease included patients aged ≥50 years with at least 1 of the following: hematochezia, melena, a change in bowel function, or positive fecal occult-blood testing.
Methods: All patients underwent colon preparation specific for the capsule. Once ingested, the cameras recorded images for the first 3 minutes, then went into "sleep mode" for 1 hour and 45 minutes (to conserve battery). Colonoscopy was performed either after capsule excretion or at least 10 hours after ingestion. The accuracy of capsule endoscopy to detect polyps, advanced adenomas, or cancer was then determined using colonoscopic results as the standard.
Results: 320 patients were analyzed in the accuracy calculations. At 1 hour and 45 minutes, the capsule was still proximal to the colon in 97.5% of patients, but was excreted within 10 hours in 93.0% of patients (with a mean total transit time of just under 5 hours). The prevalence of lesions detected by colonoscopy was 27% for any polyp >6 mm and 6% for cancer. The sensitivity/specificity of capsule endoscopy for identifying these lesions was: for any polyp >6 mm, 64%/84%, and for cancer, 74%/74%. Detection rates were better when the colon preparation was good or excellent.
Conclusions: Capsule endoscopy can be used to visualize the colon without sedation or insufflation, but its sensitivity to identify colonic lesion is approximately 65% to 75%.
Reviewer's Comments: It does appear that, although feasible, capsule endoscopy misses quite a few lesions seen on colonoscopy. It is important to note, however, that this trial was not a typical screening population, but rather a high-risk group. Therefore, we still do not know how capsule endoscopy would perform in an average-risk group. Until further information becomes available, I would recommend continuing to use colonoscopy as the primary screening test for colorectal cancer. However, in patients unable to undergo this invasive test, capsule endoscopy can deliver useful information. (Reviewer-Mark E. Pasanen, MD).

Keywords: Capsule Endoscopy, Colorectal Cancer Screening, Colonoscopy

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Famotidine Reduces Incidence of Aspirin-Induced Ulcers

Famotidine for the Prevention of Peptic Ulcers and Oesophagitis in Patients Taking Low-Dose Aspirin (FAMOUS): A Phase III, Randomised, Double-Blind, Placebo-Controlled Trial.

Taha AS, McCloskey C, et al:

Lancet 2009; 374 (July 11): 119-125

Famotidine is effective in the prevention of gastric and duodenal ulcers, and erosive esophagitis in patients taking low-dose aspirin.

Background: Proton pump inhibitors (PPIs) are effective in preventing aspirin-induced ulcers, but have a number of undesirable adverse effects.
Objective: To determine if the histamine H_2-receptor blocker famotidine (Pepcid®) is effective in preventing ulcers in patients taking low-dose aspirin.
Design: Randomized, double-blind placebo-controlled trial.
Participants: 404 patients from cardiovascular, diabetes, and stroke clinics at a hospital in England were evaluated. Patients had to be taking aspirin between 75 and 325 mg/day, and underwent an initial endoscopy to ensure they did not have ulcers or erosive esophagitis at baseline.
Methods: Patients were randomized to receive famotidine 20 mg twice daily or placebo twice daily. Patients had a follow-up endoscopy at 12 weeks, and the primary end point was development of new ulcers in the stomach or duodenum or erosive esophagitis.
Results: The authors saw a 5-fold reduction in ulcers and esophagitis in the famotidine-treated group compared to the placebo group. The absolute risk reduction was 27%, (number needed to treat, 3.70). The rate of upper gastrointestinal bleeding was also lower in the treatment group, with zero bleeds compared to 4 in the placebo group. However, in such a small study, this result could easily be due to chance.
Conclusions: According to the authors, "famotidine is effective in the prevention of gastric and duodenal ulcers, and erosive esophagitis in patients taking low-dose aspirin. These findings widen the therapeutic options for the prevention of gastrointestinal damage in patients needing vascular protection."
Reviewer's Comments: It is a little bit difficult to interpret the results of this study. It shows a large reduction in end point of small significance. Endoscopically identified ulcers that neither bleed nor cause symptoms are of minimal clinical relevance. What we care about are symptoms and bleeding, but this trial was too small to detect differences in either. It is very likely that a substantial reduction in ulcers is seen with treatment and does correlate to a reduction in symptoms and bleeding over a longer term or in a larger cohort. Looking back in the literature, there have been similar studies using PPIs that also show number needed to treat in the low single digits. On the whole, I think this study is helpful because it makes a good case for using famotidine first line in preventing ulcers in patients taking aspirin for cardiovascular protection. Famotidine is much cheaper and easier to obtain than most PPIs: it is over-the-counter in the United States, and discount stores may stock it for less than $5 for a 1-month supply. Twice-daily dosing is a problem, although patients may already be taking cardiovascular medications with similar dosing. Even if cost is not the issue, problems with clopidogrel interactions are going to be endemic in this population, which is one more reason to avoid PPIs. For now, it makes sense to use the famotidine for aspirin prophylaxis, and to save PPIs for treatment of ulcer disease or severe symptoms. (Reviewer-Christopher L. Knight, MD).

Keywords: Aspirin Ulcers, Low-Dose Aspirin, Famotidine

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Risky Business -- Hospital-Acquired MRSA Transmission to Home Is Common

Carriage of Methicillin-Resistant Staphylococcus aureus in Home Care Settings: Prevalence, Duration, and Transmission to Household Members.

Lucet JC, Paoletti X, et al:

Arch Intern Med 2009; 169 (August 10): 1372-1378

Twenty percent of household contacts of patients colonized with methicillin-resistant *Staphylococcus aureus* at hospital discharge became at least intermittent carriers, although none developed clinically significant infection.

Objective: To report the rate of and risk factors for transmission of methicillin-resistant *Staphylococcus aureus* (MRSA) to household contacts of colonized patients.
Design: Prospective cohort study.
Participants: 148 patients who screened positive for MRSA carriage at discharge.
Methods: Patients who were to receive home health services following discharge from 1 of 47 Paris hospitals were screened for MRSA carriage with cultures from the nose and/or open skin wounds. In total, 191 of 1501 screened patients were positive for MRSA, and 148 patients consented and were included in the study. Surveillance cultures were done on patients and on their household contacts (defined as being in the same house >8 hours/day) every month until discharge from home health, then every 3 months. Any cultures negative for MRSA were repeated a week later, and if culture remained negative, MRSA was defined as cleared and no further cultures were done.
Results: Mean age of patients was 70 years, and 85% had skin lesions. Clearance of MRSA occured within 1 year in 50% of patients, and 20% had persistent carriage. The remaining patients died, required a higher level of care, or withdrew consent. The only patient characteristic associated with clearance of MRSA was ability to perform activities of daily living independently. Of patients' 213 household contacts, 188 agreed to participate in the study. Overall, 19% of household contacts had a positive MRSA culture over the course of the study, although none had a clinically significant MRSA infection. The antibiotic susceptibility of MRSA isolates from each patient and household contact pair were compared, and in all cases found to be identical. Among household contacts, older age and providing care for the index patient were associated with higher rates of MRSA carriage.
Conclusions: Transmission of MRSA from patient to household contacts, particularly caregivers, is fairly common. The authors recommend that household contacts use infection control measures similar to those used during hospitalization.
Reviewer's Comments: Thankfully, the rate of clinical MRSA infection for these household contacts was zero. It is probably not practical to gown for every contact with a patient or his surroundings if you live with him, but frequent handwashing and gloves for contact with bandages or non-intact skin would be reasonable recommendations for household care providers. (Reviewer-Karen A. McDonough, MD).

Keywords: Methicillin-Resistant*Staphylococcus aureus,*Home Care Setting

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Mortality Risk Reduced When HIV Patients Undergo Susceptibility Testing

The Association of HIV Susceptibility Testing With Survival Among HIV-Infected Patients Receiving Antiretroviral Therapy: A Cohort Study.

Palella FJ Jr, Armon C, et al:

Ann Intern Med 2009; 151 (July 21): 73-84

In this cohort study, use of susceptibility testing was independently associated with improved survival among HAART-experienced patients.

Background: Among patients infected with the human immunodeficiency virus (HIV), antiretroviral susceptibility testing (ST) is now recommended for patients treated with highly active antiretroviral therapy (HAART) who have not achieved an optimal response and prior to initiating HAART for treatment-naïve patients. It is not known whether ST is associated with reductions in HIV mortality.
Objective: To determine whether ST influences HIV-related mortality among a cohort of HIV-infected patients.
Methods: The authors studied patients from the HIV Outpatient Study (HOPS), a prospective cohort of HIV-infected adults across the U.S. Since its inception in 1993, HOPS has collected data on >8000 patients and 280,000 clinical encounters. For this study, the authors selected patients who were seen in clinic at least once between 1999 and 2005 and had at least 1 measure of HIV RNA >1000 copies/mL. The principal outcomes were HIV-related mortality and morbidity rates for patients with and without ST.
Results: 2699 patients were included in the study, 915 (34%) had ST and 1784 (66%) did not. Most patients in the cohort were HAART-experienced (2107 of 2699 [78%]). Patients were followed for a median of 3.3 years. The overall mortality rate for the cohort was 2.5 deaths/100 person-years. Adjusting for potential confounders, patients who underwent ST had a lower mortality rate than patients who did not (adjusted hazard ratio (HR), 0.69; 95% CI, 0.51 to 0.94. The reduction in risk for mortality was statistically significant in HAART-experienced patients and in patients who had been heavily exposed to different HAART regimens and remained persistently viremic. There was a reduction in risk for mortality among HAART-naïve patients, although there were few deaths in this cohort subgroup and the results were non-significant. Antiretroviral regimen was changed in 95% of subjects who underwent ST compared with 75% among patients without ST.
Conclusions: There is a reduction in mortality associated with testing for antiretroviral susceptibility among patients with HIV viremia.
Reviewer's Comments: This study provides evidence in support of the current clinical practice. A randomized trial would provide stronger evidence than this cohort study, but is unlikely, given the now guideline-based approach to susceptibility testing. There is rationale for susceptibility testing, even if it does not benefit the individual, as ST may reduce the probability of developing more resistant strains of HIV that pose public health risks. (Reviewer-Paul R. Sutton, PhD, MD).

Keywords: Susceptibility Testing, Highly Active Antiretroviral Therapy, Mortality

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Are Repeat EIA Tests Necessary for *C diff* Diarrhea?

Diagnostic Value of Repeated Enzyme Immunoassays in Clostridium difficile Infection.

Nemat H, Khan R, et al:

Am J Gastroenterol 2009; 104 (August): 2035-2041

In a single institution retrospective study, repeated enzyme immunoassays for *Clostridium difficile* toxins A and/or B were of low yield. The authors recommend a single stool specimen, except in selected cases.

Background: Testing for *Clostridium difficile*-associated diarrhea (CDAD) is generally done with commercial enzyme immunoassays (EIAs), which offer rapid turnaround, but are less sensitive than the gold standard *C difficile* toxin A&B and stool cytotoxin assay. The sensitivity of the most commonly used EIA for the toxin A antigen has a sensitivity that ranges in published studies from 63% to 99%, but in common clinical practice has a sensitivity in the 85% to 90% range; there is also an EIA for the less common *C difficile* toxin B. Thus, false-negative *C difficile* toxin EIAs are potentially problematic, particularly in light of the important issues surrounding infection control procedures in hospitals.
Objective: To evaluate the diagnostic utility of second and third EIAs for the detection of *C difficile* toxins A and B in the diagnosis of CDAD.
Design/Methods: This was a retrospective single institution study of all stool EIAs ordered for suspected CDAD over a 3.5-year period. Multiple stool studies ordered within a 5-day period were defined as repeat stool EIAs for a single episode of suspected CDAD. The primary outcome was the diagnostic yield of repeated EIAs in the evaluation of suspected CDAD.
Results: 3712 patients and 5865 separate episodes of diarrhea were included in the study; 9178 stool samples were ordered, for an average of 1.56 stool samples per episode. The first sample was positive for toxin A in 17.83% of cases. Of 4819 patients with a negative initial toxin EIA, a second assay was ordered in 1934 cases (40.1%). Of these, 95 or 4.9% were positive (95% CI, 3.99 to 5.97%). Of 1839 patients with a negative second EIA, a third assay was ordered in 793 cases (43.1%), and was positive in 24 (3.0%; 95% CI, 1.95 to 4.47). Of 1165 patients diagnosed with CDAD, 89.8% were diagnosed with the first EIA, 8.2% with the second, and 2.0% with the third.
Conclusions: Repeat EIA testing for CDAD was of low yield.
Reviewer's Comments: There has been an evolution away from the practice of ordering multiple stool samples for suspected CDAD in my own hospital-based practice, based largely on the advice of our laboratory medicine department that the yield is low (little added utility for the additional cost). This study supports this practice. As the authors suggest, however, there are individual clinical situations where it may be appropriate to send additional stool samples, such as patients with flares of inflammatory bowel disease where the pre-test probability of CDAD is higher, or critically ill immunocompromised patients. (Reviewer-Paul R. Sutton, PhD, MD).

Keywords:*Clostridium difficile*-Associated Diarrhea, Enzyme Immunoassay, Diagnostic Utility

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Meta-Analysis Links Travel, Risk of VTE

Meta-Analysis: Travel and Risk for Venous Thromboembolism.

Chandra D, Parisini E, Mozaffarian D:

Ann Intern Med 2009; 151 (August 4): 180-190

In this meta-analysis, travel was associated with a 2- to 3-fold increased risk of venous thromboembolism. There was a dose-response relationship between duration of travel and increased risk.

Background: Has a patient ever asked you about the risk of blood clot associated with travel? A potential association has biological plausibility, as long distance travel by air, train, bus, or car involves greater stasis than one likely encounters in everyday life. Air travel adds the additional potential risk factor of relative hypoxia-induced hypercoagulability. Epidemiological studies published to date have drawn varying conclusions about the potential association between travel and venous thromboembolism (VTE).
Objective: The current meta-analysis was designed to evaluate the magnitude of the association between travel and VTE.
Methods: The authors searched for all epidemiological studies that estimated the magnitude of association between travel by any means and VTE. Included studies were observational studies or clinical trials. The authors estimated the relative risk (RR) for VTE among travelers and nontravelers.
Results: The 14 studies in the meta-analysis included 4055 cases of VTE. There was significant heterogeneity among studies. Seven of the studies found an association between travel and VTE and 7 did not. When pooled, the RR for VTE among travelers was 2.0 (95% CI, 1.5 to 2.7; P <0.001). Among the studies the authors identified as most methodologically sound, the estimated RR for VTE among travelers was 2.8 (95% CI, 2.2 to 3.7). The estimate of risk of VTE was slightly higher among air travelers compared with surface travel (RR, 1.4; 95% CI, 1.0 to 2.1), but the difference was not statistically significant. Among the subset of studies that reported duration of travel, there was a dose-response association with an 18% higher risk of VTE for each 2-hour increase in the duration of travel (95% CI, 4% to 33%; P =0.010).
Conclusions: There is a 2- to 3-fold higher risk of VTE among travelers compared with nontravelers. The risk increases with longer trips.
Reviewer's Comments: This was a methodologically well-done meta-analysis. Nonetheless, it is notable that 1 of 2 previously published meta-analyses found no association between travel and VTE. While this study cannot be regarded as proof of an association between travel and VTE, the biological plausibility and the apparent dose-response are compatible with a cause-and-effect relationship. This study lends credence to a clinical approach that considers recent travel and duration of travel in estimating prior probability of VTE, even if not formally a part of the commonly used Wells or Geneva risk scores. (Reviewer-Paul R. Sutton, PhD, MD).

Keywords: Travel Venous Thromboembolism, Hypercoagulability, Meta-Analysis

Print Tag: Refer to original journal article

Do ACEI/ARBs Protect Kidneys in Normotensive Type 1 Diabetics?

Renal and Retinal Effects of Enalapril and Losartan in Type 1 Diabetes.

Mauer M, Zinman B, et al:

N Engl J Med 2009; 361 (July 2): 40-51

In normotensive type 1 diabetics without evidence of kidney disease, the addition of renin-angiotensin blockade does not affect progression of diabetic kidney disease.

Background: In patients with diabetes mellitus, it is standard practice to initiate treatment with renin-angiotensin blockade at the first sign of excess protein excretion. However, although effective in reducing the progression of proteinuria, there is not convincing evidence showing a change in the rate of decline in glomerular filtration rate (GFR).
Objective: To determine whether renin-angiotensin blockade in normotensive type 1 diabetics without evidence of kidney disease would affect renal histology (as a marker for progression of nephropathy). In addition, the stage of retinal disease was monitored.
Design: Randomized double-blind placebo-controlled clinical trial.
Participants: Patients aged ≥18 years with type 1 diabetes, blood pressure <130/85 mm Hg, and no evidence of microalbuminuria were eligible.
Methods: After baseline kidney biopsies and retinal exams were performed, patients were randomly assigned to enalapril (Vasotec®) 10 to 20 mg daily, losartan (Cozaar®) 50 to 100 mg daily, or placebo for 5 years. Every 3 months, glycemic control, renal function, blood pressure, and urinary protein excretion were monitored. After 5 years of treatment, kidney biopsies and retinal exams were repeated. The primary end point was a measurement of mesangial occupation of glomeruli, an early histologic manifestation of diabetic nephropathy.
Results: 285 patients were enrolled, with an average age of 30 years and average duration of diabetes of 11 years. After 5 years, there were no significant histologic differences between the 3 groups nor were there differences in GFR. The cumulative incidence of microalbuminuria was similar in the placebo and enalapril arms, and was actually higher in the losartan group. As for retinopathy, roughly two thirds had evidence of some degree of diabetic retinopathy at baseline. The addition of either enalapril or losartan decreased the likelihood of significant progression over 5 years.
Conclusions: In normotensive type 1 diabetics without evidence of kidney disease, the addition of renin-angiotensin blockade does not affect the progression of diabetic kidney disease. However, it does appear to slow the rate of progression of diabetic eye disease.
Reviewer's Comments: Given that kidney and eye disease remain major areas of concern in diabetes, interventions to prevent or slow these complications are critical. However, progression of kidney disease takes many years, making it difficult to study. Most efforts have looked at albuminuria as a surrogate measure for renal status. Although a good marker for kidney disease, reduction in albuminuria has not been a particularly good surrogate marker for accurate prediction of future renal function. This study utilized kidney biopsy as an alternate, and perhaps, more accurate way to measure the impact of interventions on prevention of progressive kidney disease. Unfortunately, neither ACEI nor ARB showed any benefit over 5 years on nephropathy, but did help slow down eye disease. Therefore, I think the role of these agents in normotensive diabetics remains unclear. (Reviewer-Mark E. Pasanen, MD).

Keywords: Diabetes Mellitus, Retinopathy, Nephropathy, ACE Inhibitors, Angiotensin-Receptor Blockers

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Stroke Risk Not Increased by Chronic Beta-Blocker Use

Effect of Chronic Beta-Blocker Use on Stroke After Noncardiac Surgery.

van Lier F, Schouten O, et al:

Am J Cardiol 2009; 104 (August 1): 429-433

Contrary to the POISE trial results, patients treated chronically with beta-blockers were not at increased risk of perioperative stroke in this study.

Background: Over the past 15 years, several studies have shown that beta-blockers decrease the risk of perioperative cardiac complications in higher risk patients. But in the 2008 PeriOperative ISchemic Evaluation (POISE) trial, in which patients were randomized to high-dose metoprolol (DutoprolTM) or placebo begun just before surgery, found that the beta-blocker group had a significantly increased risk of stroke.
Objective: To define the risk of perioperative stroke in patients treated chronically with beta-blockers.
Design: Case-control study.
Participants: 34 patients who suffered a stroke within 30 days of noncardiac surgery (excluding intracerebral or carotid surgery).
Methods: The authors searched the computerized medical records of almost 187,000 surgical patients from a single Dutch hospital from 2000 to 2007 for the terms "stroke," "transient ischemic attack," or "cerebrovascular accident." They reviewed all cases identified, and found 34 case patients. They assigned 2 controls to each case, of the same age, gender, year, and type of surgery. Comorbid illness, medication list, and duration of beta-blocker use were determined from the medical records. Beta-blocker use >30 days was defined as chronic.
Results: The overall risk of stroke appeared to be very low (0.05%). In both cases and controls, the most common surgeries were esophageal and abdominal (39%); orthopedic (32%); ear, nose, and throat (9%); and vascular (9%). A history of cerebrovascular disease was associated with a significantly higher risk. The stroke patients were no more likely to be receiving a beta-blocker (29% of stroke patients and 29% of controls were taking one, all chronically).
Conclusions: Patients treated chronically with beta-blockers were not at increased risk of perioperative stroke.
Reviewer's Comments: The increased stroke risk seen with beta-blockers in POISE is probably due, at least in part, to bradycardia and hypotension from initiation of a high dose just before surgery. This case-control study reassures me that chronically treated patients are not at increased risk. Of course, even after POISE, there has been general agreement that patients on beta-blockers should certainly not STOP them in anticipation of surgery, because of the increased risk of cardiac complications associated with withdrawal. (Reviewer-Karen A. McDonough, MD).

Keywords: Perioperative Beta-Blockade, Stroke, Noncardiac Surgery

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Consider Treatable Causes of Insomnia Before Prescribing Meds

Sleep and Sleep Disorders in Chronic Users of Zopiclone and Drug-Free Insomniacs.

Sivertsen B, Omvik S, et al:

J Clin Sleep Med 2009; 5 (August): 349-354

Evaluate people with chronic insomnia for anxiety, depression, and sleep apnea before prescribing a long-term sleep medication, as these are common and treatable underlying causes of insomnia.

Background: In studies that exclude patients with identifiable causes for insomnia, zopiclone (Lunesta®) is effective for chronic insomnia. Sleep medications are increasingly prescribed with unknown efficacy for chronic insomnia in the general population.
Objective: To evaluate sleep quality and quantity in older insomniacs on zopiclone for ≥1 year.
Participants/Methods: Subjects aged ≥55 years were recruited through newspaper advertisements; participants meeting criteria included 17 people using zopiclone for ≥1 year, 26 people with insomnia but no sleep medications for ≥4 weeks, and 26 healthy people with self-reported good sleep. All underwent 2 nights of polysomnograms, completed sleep diaries for 2 weeks, and completed standard anxiety and depression questionnaires.
Results: Chronic zopiclone users slept no better than non-medicated insomniacs and had higher scores on anxiety and depression scales than the non-medicated insomniacs, who scored higher on those scales than good sleepers. Sleep apnea (apnea-hypopnea index >10 events/hour) was identified in 41% of zopiclone users and in 42% of non-medicated insomniacs compared with 12% of good sleepers.
Conclusions: Chronic use of zopiclone does not objectively improve sleep in insomniacs treated in the community. Physicians should evaluate patients for specific causes of persistent insomnia, including sleep apnea and mood/anxiety disorders, before prescribing long-term use of a sleep medication.
Reviewer's Comments: People increasingly seek relief from physicians for the symptom of insomnia. Marketing to consumers and physicians doesn't stress that insomnia can have an identifiable, treatable cause. This study has some limitations, including not reporting whether zopiclone users slept worse without the drug, were satisfied with their treatment, or might have previously failed treatment for anxiety, depression, or sleep apnea. However, this study demonstrates that undifferentiated pharmaceutical treatment of "insomnia" may not have the same beneficial effects as in carefully controlled conditions, and that sleep apnea, anxiety, and depression are common in people seeking treatment for chronic insomnia. (Reviewer-Eliza L. Sutton, MD).

Keywords: Insomnia, Sleep Apnea, Hypnotic Medications, Zopiclone

Print Tag: Refer to original journal article

Professional Societies Set Standards for Transitions Between Inpatient, Outpatient Care

Transitions of Care Consensus Policy Statement: American College of Physicians, Society of General Internal Medicine, Society of Hospital Medicine, American Geriatrics Society, American College of Emergency Physicians, and Society for Academic Emergency Medicine.

Snow V, Beck D, et al:

J Hosp Med 2009; 4 (July): 364-370

A number of professional societies have joined together to develop a consensus statement on how to optimize patient care and safety at times of transition of care between inpatient and outpatient settings.

Background: Transitions between inpatient and outpatient care are particularly vulnerable to adverse events, including medication error, inadequate follow-up of pending test results, and loss of information because of inadequate communication between physicians and patients and among inpatient and outpatient physicians.
Objective: To address the quality gaps in the transitions between inpatient and outpatient settings and to develop consensus standards for these transitions.
Design/Methods: This paper was a consensus statement that resulted from the Transitions of Care Consensus Conference (TOCCC), involving experts from the American College of Physicians, Society of General Internal Medicine, Society of Hospital Medicine, American Geriatric Society, American College of Emergency Physicians, and Society of Academic Emergency Medicine.
Results: A number of guiding principles were developed by the TOCCC, including accountability, timeliness of communication congruent with the timing of follow-up, clear and direct communication between providers, involvement of patients and family members, and clear identification by physicians, patients, and families of who is immediately responsible for the care of the patient at every point in time. The TOCCC also recommended identifying standardized metrics related to the quality of transitions of care, such as standard data elements that should be included in all transition records.
Conclusions: Based on these metrics, the TOCC recommends establishing national standards for transitions of care that would be widely adopted by health care organizations and subject to evaluation by licensing and accrediting bodies.
Reviewer's Comments: The growing focus on patient safety has drawn attention to transitions of care between the inpatient and outpatient arenas. Recent studies have found that adverse events such as medication errors are common, timeliness of communication is suboptimal, and information is lost. This consensus statement represents an early foray into developing standardized approaches to improving patient safety and health outcomes at transitions of care. Substantial challenges clearly remain, such as changes in health care delivery that help patients have primary care or improvements in health information systems that model standardized transition of care reports. (Reviewer-Paul R. Sutton, PhD, MD).

Keywords: Transitions of Care, Discharge Coordination

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