Occupational history is documented in approximately 50% of patients with newly diagnosed chronic bronchitis.

**Background:** The authors of this paper have previously demonstrated that occupational histories were not adequate in patients with a diagnosis of asthma. They therefore wondered whether this trend might be seen in patients with chronic bronchitis as well.

**Objective:** This study was conducted at a Veterans Administration health care center.

**Participants/Methods:** Patients who are directed to the pulmonary function laboratory typically fill out a questionnaire regarding their respiratory history. The medical records of the patients were reviewed between 1999 and 2008. All patients were between 18 and 70 years of age and had a newly reported diagnosis of chronic bronchitis. All patients underwent pulmonary function testing, and all had completed a pulmonary function test laboratory questionnaire. The authors then searched the medical record for identification of occupational history.

**Results:** 580 patients with a new diagnosis of chronic bronchitis were identified. Of these, 354 patients had completed pulmonary function tests, and of these, 141 had completed the questionnaire. Subsequently, only 60 of the patients met the pre-specified age inclusion criteria. Eighty-eight percent of the patients were men, with an average age of 60 years; 42% were current smokers. The average FEV₁ was 55%. Over 6000 notes from health care providers were reviewed. Occupational history that included specific work duties was identified in approximately 50% of the subject patients. This documentation included the presence of potential exposures to fumes or gases at work. Linkage of occupational exposure to the causation of the bronchitis was rare. Only 3 patients had such a notation in their medical records. Six patients received advice to avoid exposures and 1 patient was referred to a claims board. Smoking status, pulmonary function, nor demographic characteristics predicted a history of occupational exposure that was documented by the clinician. Approximately 58% of the patients reported a history of occupational exposures to gases or fumes on the self-administered patient pulmonary function test questionnaire.

**Conclusions:** The authors conclude that occupational history was documented in approximately 50% of the patients with newly diagnosed chronic bronchitis. Self-report of occupational exposure was common. A linkage between occupational exposure and disease was rare.

**Reviewer’s Comments:** These data exemplify something that I have seen currently in the house staff and fellows that rotate through my ICU. The art of history taking has taken a backseat to diagnostic testing. (Reviewer-Eric H. Gluck, MD, JD).

© 2009, Oakstone Medical Publishing

Keywords: Occupational Diseases

Print Tag: Refer to original journal article
Objective: To evaluate an association between life expectancy and fine particulate air pollution.

Methods: Data were acquired from 51 United States cities and compared for the time from the late 1970s to the early 1980s with matched data from the late 1990s to the early 2000s. From 1979 to 1983, the Environmental Protection Agency (EPA) maintained a database that included measurements of 15 μm and 2.5 μm of particulate matter in the air. Subsequent to 1983, the database was discontinued, but was reinstated in 1997 under the National Ambient Air Quality Standard for particulate matter 2.5 (PM$_{2.5}$). Daily data for PM$_{2.5}$ were available for 1999 and for the first 3 quarters of 2000. Standard life table techniques were used to estimate the annual life expectancies for >2000 individual or merged counties in the United States. Data for life expectancy were collected into different pools of data from 1978 through 1982 and from 1997 through 2001.

Results: The PM$_{2.5}$ concentrations declined during the 1980s and the 1990s, but life expectancy increased between the 2 time periods. This was true when the data were analyzed based on county or metropolitan area observations. An increase in PM$_{2.5}$ concentration of 10 μg was associated with a reduction in life expectancy of about 1.19 years during the time period of 1978 to 1982 and 2.02 years during that time period of 1997 through 2001. Areas with more significant reduction in air pollution experienced greater increases in life expectancy. The improvement in life expectancy was not very sensitive after adjustment for changes in social, economic, and demographic variables. In addition, even when correcting for the prevalence of smoking or restricting the observations to very large counties, the effect on reduction in PM$_{2.5}$ was quite significant. The data demonstrated that an improvement in air pollution accounted for approximately 15% of the overall increase in life expectancy seen in the areas under investigation.

Conclusions: A reduction in exposure to PM$_{2.5}$ in diameter has contributed to a significant improvement in life expectancy in the United States.

Reviewer's Comments: We have previously reported in this journal that air pollution is associated with increased risk for asthma exacerbations, chronic obstructive pulmonary disease exacerbations, and bronchitis. Data were also presented that suggested that improvement in air pollution improves quality of life. I believe these are the first data that we present in this journal that demonstrates that life expectancy can be improved in areas where air pollution is reduced. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Pollution

Print Tag: Refer to original journal article
ARDS Mortality Is Stagnant

Has Mortality From Acute Respiratory Distress Syndrome Decreased Over Time? A Systematic Review.
Phua J, Badia JR, et al:
Am J Respir Crit Care Med 2009; 179 (February 1): 220-227

In a regression analysis, the only factors that appear to be related to mortality are the patient's age and whether the study was published before or after the change in definition of ARDS.

Objective/Design: To a meta-analysis of the literature to determine whether there has been a significant mortality improvement in acute respiratory distress syndrome (ARDS) in the United States.

Methods: The authors searched multiple different medical databases for articles relevant to ARDS and survival from 1984 through November 2006. Independent reviewers looked at the articles for relevancy and meeting the criteria that was set for the study. Studies were selected if they included prospective observational data for randomized controlled trials with ≥50 adults. Any definition for acute lung injury (ALI) and for ARDS were used as long as they reported mortality. Six pairs of independent reviewers assessed the methodology of the study and extracted the data. The initial review of the database yielded almost 5000 articles. After appropriate exclusions, the final selection included 89 studies, 85 of which were published in English and the rest in foreign languages. The studies included almost 19,000 patients. There was a preponderance of observational studies over randomized controlled trials.

Results: The pooled weighted mortality rate from the studies published between 1984 and 2006 was 44%. Mortality rate was slightly higher in observational studies than in randomized controlled trials. There was significant heterogeneity for mortality across all the studies. Visual inspection of mortality rate as a function of year of study suggested that there was a slight decrease in mortality over time. This effect, however, appears to be also a function of the new definition of ARDS that was identified in 1994. The mortality rate for observational studies was 44% and 36% for randomized controlled trials. In a regression analysis, the only factors that appeared to be related to mortality were the patient's age and whether the study was published before or after the change in definition. In a third meta-regression model, which included all 89 studies, mortality was associated with the type of study (with observational studies having a higher mortality rate), the age of the patient, and the date of the study.

Conclusions: A decrease in ARDS mortality was seen in observational studies between 1984 and 1993. There does not appear to have been a further reduction in mortality rates between 1994 and 2006.

Reviewer's Comments: Interestingly, these data, unfortunately, appear to show that we have reached a plateau in mortality rates for patients with ARDS. (Reviewer-Eric H. Gluck, MD, JD).

© 2009, Oakstone Medical Publishing

Keywords: Mortality

Print Tag: Refer to original journal article
There appears to be a statistically significant difference favoring anti-infective central venous catheters, with an odds ratio of reducing infection of 0.49.

**Design/Objective:** This was a review of articles published in the medical literature that dealt with catheter-related bloodstream infections (CRBSIs) and preventative measures.

**Methods:** The articles were reviewed for potential eligibility and selected by 2 investigators. Data were then extracted by these 2 investigators independently, and a meta-analysis was performed.

**Results:** The authors report that the methodology quality of the studies was quite poor, with >50% of the studies failing to identify method of randomization, allocation concealment, and blinding procedures. Twenty-eight of the 38 included studies compared standard central venous catheters (CVCs) with anti-infective CVC (AI-CVCs) and provided rates of CRBSIs. Impregnated cuff technology considered a different technology and was not included in the analysis. The meta-analysis of all the trials suggested a statistically significant difference favoring AI-CVCs, with an odds ratio of reducing infection of 0.49. When the studies were further broken down with respect to the type of AI methodology, catheters treated with AI agents (except for benzalkonium chloride) also demonstrated favorable outcomes. The latter, however, did not, but perhaps this was because the study size was small. Likewise, subgroup analysis based on patient type, diagnosis duration, and insertion site all demonstrated favorable outcomes for the treated catheters. Overall, the meta-analysis demonstrated a reduction of 60% in the rate of catheter-related septic episodes per 1000 days of treatment compared with standard catheters.

**Conclusions:** AI-CVCs appear to be effective in reducing infection compared with standard catheters. However, it should be noted that many of the studies preceded the use of AI bundles, which might actually change the outcomes of some of the studies.

**Reviewer's Comments:** There are 2 significant issues that need to be addressed besides reporting the significant improvement in outcomes. Treated catheters typically are more expensive, and some patients may have adverse reactions to the chemicals that are impregnated in the walls of the catheter. This being placed aside, these data strongly suggest that catheters that are treated can significantly reduce a potentially lethal complication associated with CVCs. Obviously, keeping in catheters for the shortest period of time, as well as not placing catheters unnecessarily, would also add to the benefit of this program. Until we find an alternative for administering medications and monitoring patients, it would appear that the use of AI-CVCs would significantly benefit our patients. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Central Venous Catheters

Print Tag: Refer to original journal article
There are acute and reversible left ventricular dilation associated with septic shock that induces systolic left ventricle dysfunction.

Objective: To evaluate whether cardiac ventricles acutely dilate during septic myocardial dysfunction.
Participants/Methods: To identify the nature of the cardiac dysfunction associated with sepsis, 53 patients admitted to a surgical ICU for septic shock were enrolled in a prospective study. A subgroup of 45 patients who survived the first 10 days was used to analyze changes in left ventricular dimensions. All of the patients required some form of vasopressor or inotropic agent for support, and all were receiving controlled ventilation. Typical goals for ventilatory therapy were followed. Group 1 consisted of 29 patients who had troponin levels <0.2 ng/mL without septic shock-induced cardiac impairment. Group 2 consisted of 8 patients with a reversible increase in troponin and reversible left systolic ventricular dysfunction. Group 3 included 8 patients with an increase in troponin and a left ventricular ejection fraction ≥50%, but with impairment of left ventricular relaxation. Patients were studied from the onset of septic shock for a period of 10 days. Transesophageal echocardiograms were performed on all patients.
Results: In group 1 patients, the echocardiogram remained unchanged throughout the study. In group 2 patients, the echocardiographic changes returned to baseline by day 10. Left ventricular end diastolic area increased statistically in patients who had increased levels of troponin. Systolic artery pressures were no different throughout the study in all 3 groups. Also, patients who have elevated troponin levels and a fractional area change of <50% had their hemodynamic parameters return to normal by the end of the study.
Conclusions: There are acute and reversible left ventricular dilation associated with septic shock, which induces systolic left ventricle dysfunction. In addition, there are some patients who have impairment of left ventricle relaxation.
Reviewer's Comments: The take-home message from the study is that a significant percentage of patients with septic shock will develop left ventricular dysfunction. Despite the fact that the left ventricle is restricted in part by the pericardium, there appears to be the ability to develop dilation. In addition, some patients demonstrate significant relaxation abnormalities. Since the type of volume resuscitation that would be beneficial to patients with these 2 different types of ventricular impairments is different, evaluation of fluid resuscitation needs to be individualized. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Acute Left Ventricular Dilatation

Print Tag: Refer to original journal article
Immunosuppression does not affect the sensitivity of the immunoassay for tuberculosis even though it does have a significant adverse affect on skin testing.

**Background:** Tuberculosis may present outside of the chest in both immunocompetent and immunocompromised patients. The latter, however, present a diagnostic conundrum because of a poor reactivity to the skin testing for tuberculosis. Patients need to be treated aggressively and early in order to prevent significant morbidity from this disease. An enzyme linked immunospot assay detecting interferon gamma secreting T-cells is based on 2 different antigens. The assay has recently demonstrated promising results. In addition, some reported preliminary data suggest as an adjunct test it is useful in diagnosing extra pulmonary tuberculosis with a sensitivity reaching >90%. However, data in immunocompromised patients are lacking to date.

**Objective:** To evaluate its use in this group of patients.

**Participants/Methods:** All patients with suspected tuberculosis outside of the chest cavity were enrolled in a university hospital setting in South Korea between 2006 and 2007. Standard techniques were used for processing microbiological material. Treatment was solely at the discretion of the clinician. Standard procedure was used for collecting blood and performing the immunoassay. The results of the skin test and immunoassay were not concealed from the physicians during our evaluation. There were 186 subjects who were suspected of having extrapulmonary tuberculosis. All subjects received both the skin test and the immunoassay. Three patients who had an indeterminate result from immunoassay and 4 patients who missed follow-up visit were excluded leaving 179 patients. 33% of these patients were classified as immunocompromised. When the investigators removed patients with possible tuberculosis from the analysis, leaving only the patients with probable or definite tuberculosis, the sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio of the skin test was 59%, 76%, 66%, 70%, respectively. The results for the immunoassay were significantly better at 93%, 66%, 68%, 93%, respectively. The positive and negative likelihood ratios were 2.47 and 0.54 and 2.74 and 0.10, respectively. These data were for the entire group. When the data were evaluated for patients who were immunocompromised, the skin test demonstrated lower sensitivity, but the immunoassay did not demonstrate a change in sensitivity.

**Conclusions:** Immunosuppression does not affect the sensitivity of the immunoassay for tuberculosis even though it does have a significant adverse affect on skin testing.

**Reviewer's Comments:** It would appear that there is a bright future for the immunoassay testing for tuberculosis, especially in patients who are immunocompromised. However, there is still significant benefit for using an assay that is purely objective over using skin testing, which at times can have a subjective bias based on the fact that individual persons might interpret induration differently. (Reviewer-Eric H. Gluck, MD, JD)

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Keywords: Diagnostics

Print Tag: Refer to original journal article
Patients with lung cancer who undergo lung resection fail to completely recover to baseline even after 24 months of follow-up.

Objective: To evaluate whether the type of surgical intervention for lung cancer might have a significant impact on quality-of-life (QOL) issues following surgery.

Participants: 159 consecutive patients treated for non-small cell lung cancer (NSCLC) at a university medical center in Germany.

Methods: Pneumonectomy was performed when the main bronchus was infiltrated by tumor. The rest of the patients received either lobectomy or bilobectomy. All patients had a mediastinal exploration with lymph node removal, with QOL assessed using a specific cancer-related 30-item questionnaire. The questionnaire included functional scales relating to physical ability, role ability, cognitive function, emotional functional status, and social status. There were also 3 scales relating to global health issues. Questionnaires were administered to patients before surgery, prior to hospital discharge, and at least on 1 occasion in the following 24 months.

Results: 131 of patients underwent either lobectomy or bilobectomy, and 28 underwent pneumonectomy. The prevailing cell type was squamous cell closely followed by adenocarcinoma and then a small percentage had large cell cancer. During the study observation time, 78 of these patients died within an overall mean survival time of 43 months. The 5-year survival rate was 42%. The mean survival time for patients with stage I cancer was 54 months. The survival time appears to be longer for patients with adenocarcinoma than for patients with squamous cell carcinoma. After discharge from the hospital, all functional scales from the questionnaire had fallen significantly below the baseline. There was a slight improvement observed at 3 months and 6 months after surgery, but these values did not achieve those of the preoperative level. In fact, most functional scales failed to reach preoperative levels even after 2 years of follow-up. Role function and social function did not appear to be adversely affected. Even symptomatology was significantly worse at 2 year follow-up than prior to surgery. Patients who underwent pneumonectomy had significantly worse functional scales than patients who went under by lobectomy. In addition, patients who underwent pneumonectomy had significant increases in the symptoms of cough, pain, and dyspnea.

Conclusions: Patients who undergo lung resection fail to completely recover to baseline even after 24 months of follow-up. Patients who undergo pneumonectomy have significantly worse QOL than patients who undergo lobectomy.

Reviewer's Comments: The major take-home message from this paper is to limit surgical intervention for lung cancer to the smallest amount of lung tissue that will successfully improve outcome, while at the same time including the patient in the decision making process so that he or she is well aware of the potential for reduction in QOL. (Reviewer-Eric H. Gluck, MD, JD).
New Marker for ARDS a Possibility

Elevated Levels of the Receptor for Advanced Glycation End Products, a Marker of Alveolar Epithelial Type 1 Cell Injury, Predict Impaired Alveolar Fluid Clearance in Isolated Perfused Human Lungs.

Briot R, Frank JA, et al:

Chest 2009; 135 (February): 269-275

Levels of RAGE are inversely associated with the ability of the lung to clear alveolar fluid.

Objective: To identify a new biomarker that may allow identification of patients with alveolar capillary leak.

Methods: The study was performed on donated organs for transplantation, which for several reasons did not result in actual transplantation into a patient. This preparation of a lung outside the body was via a cannulation by the pulmonary artery and intubation through the main stem bronchus. The pulmonary veins were not cannulated and venous drainage was allowed to occur passively. The lung was suspended and surrounded by a container that was heated to 38°C. Alveolar fluid clearance was measured continuously by instilling 150 mL of normal saline containing 5% albumin through a catheter into the airspace of the lung. After 5 minutes and then an additional 30 minutes, the protein concentration in the air spaces was used to determine the volume of fluid that had been cleared from the air spaces. The receptor for advanced glycation end products (RAGE) was then measured using an immunoassay (Technik). All of the lungs included in the study were from patients who died from a catastrophic central nervous system injury. The mean alveolar fluid clearance rate for all lungs studied was 17% ± 2%/hour. RAGE concentration differed according to the reason for rejection of the lung for transplantation. Lungs with abnormal alveolar fluid clearance had higher levels of RAGE than lungs with intact alveolar fluid clearance. There was a statistically inverse correlation between alveolar fluid clearance and RAGE levels. Alveolar fluid concentration clearance was not related to von Willebrand factor.

Conclusions: RAGE levels may be a useful biological marker for alveolar epithelial injury and associated impaired mobility fluid clearance. This technique might be useful in lungs prior to transplantation and perhaps in patients with acute lung injury.

Reviewer's Comments: Assuming that these data hold up in future studies, we might now have a better biomarker for the dedication of patients with ARDS. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Biomarkers

Print Tag: Refer to original journal article
The regular use of marijuana has been linked to development of bullous lung disease.

**Background:** Compared to tobacco smoking, there is more particulate matter that enters the lungs with marijuana smoking. Studies show there is 4 times as much tar and 50% more carcinogens in marijuana smoke compared to tobacco. On inhalation, a marijuana cigarette delivers almost twice as much smoke, has one-third greater depth of inspiration, and has a breath hold 4 times longer compared to smoking a tobacco cigarette. Tasklin and colleagues documented the association of long-term marijuana smoking with many features of obstructive lung disease, including chronic cough and bronchitis, decreased exercise tolerance, and evidence of airflow obstruction.

**Objective:** To document the association between marijuana smoking and bullous lung disease.

**Design:** Prospective study.

**Participants/Methods:** Over a 12-month period, 10 patients admitted to their hospital with respiratory complaints who had smoked marijuana regularly for at least 1 year at some time during their life were identified.

**Results:** 4 patients presented with spontaneous pneumothorax and 2 presented with lung abscess. The mean age of patients at presentation was 41 years, and all were current or former cigarette smokers. Alpha-1 antitrypsin levels were normal in all patients. Three patients had moderate to severe airflow obstruction on pulmonary function testing. Interestingly, high-resolution CT scans showed asymmetrical, variably sized bullae in 9 of the 10 patients. These bullae were located mainly in the upper and mid lung zones. They could be located in the periphery or in the central regions of the lung.

**Conclusions:** 9 of the 10 patients who smoked marijuana regularly for at least 1 year had bullous disease on high-resolution CT scan.

**Reviewer’s Comments:** These patients presented at an earlier age (mean age, 41 years) than did the patients who had smoked tobacco (mean age, 67 years). Their pulmonary function tests were not always abnormal, and their chest x-ray was not always abnormal. I think there are some who have a cavalier attitude concerning possible adverse effects of marijuana use on lung health. This report emphasizes there can be significant adverse consequences of marijuana smoking on the lung. (Reviewer-Richard A. Nusser, MD).

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Keywords: Marijuana

Print Tag: Refer to original journal article
Atrial Fibrillation Progression, Management

Atrial Fibrillation Progression and Management: A 5-Year Prospective Follow-Up Study.

Pappone C, Radinovic A, et al:

Heart Rhythm 2008; 5 (November): 1501-1507

Atrial fibrillation is a progressive disease that does not respond well to anti-arrhythmic drugs.

Background: In the era of catheter ablation of atrial fibrillation (AF), there are no prospective data assessing AF progression.

Objective: To prospectively assess progression of AF treated with anti-arrhythmic drugs (AAD) and catheter ablation.

Methods: Included were patients with a first ever episode of AF. Patients with potentially reversible causes of AF were excluded. Patients were followed for 5 years. Portable monitors recorded patients’ rhythm. Patients were not treated after a first episode of paroxysmal AF. If AF recurred, symptomatic patients were treated with AAD. If drug intolerance or failure occurred, catheter ablation was offered. Treatment efficacy was compared in AAD and catheter ablation groups. Primary end point was AF progression; also assessed were predictors of AF progression and effect of catheter ablation.

Results: Of 106 patients, 54 had lone AF and 52 had AF with ≥1 comorbidity. During follow-up, 50 patients had no further recurrences, while 56 patients had recurrent AF and were treated with AAD. Of these patients, 11 did not tolerate the AAD or had drug-refractory AF, and had catheter ablation. The other 45 patients were continued on AAD. There were no significant baseline differences between the 2 groups. Patients with catheter ablation remained free of AF after a median follow-up of 40 months. In the AAD group, 21 patients had recurrent paroxysmal AF and 24 progressed to persistent AF. Of these 24 patients, 16 progressed further to permanent AF. Of those with eventual permanent AF, all but 1 had ≥1 comorbidity. Patients with lone AF had much less progression to persistent AF. In patients with progression of AF, it took an average of 26 months to progress from the first episode to the persistent form of AF. Progression to permanent AF took only an additional 10 months on average. Baseline age, diabetes, and heart failure predicted progression to permanent AF on multivariate analysis.

Conclusions: A significant number of patients with a first episode of AF will remain free of AF at 5-year follow-up. Patients with comorbid conditions are at increased risk of AF recurrence and progression to chronic forms of AF. AAD are not very effective in halting AF progression. Catheter ablation may arrest progression and recurrence of AF.

Reviewer's Comments: This study provides interesting observations about the natural history of AF and the outcome of current management strategies. It suggests that many patients with an initial episode of AF may have no further recurrences and may not need aggressive intervention. It also suggests that the future may be kinder to ablation-based strategies compared to AAD-based ones. Larger trials are needed to confirm some of the data observed in this study. (Reviewer-Khalid Almuti, MD).

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Keywords: Atrial Fibrillation

Print Tag: Refer to original journal article
ACE Inhibitors May Be Beneficial in Select AF Pts

Prevention of Recurrent Lone Atrial Fibrillation by the Angiotensin-II Converting Enzyme Inhibitor Ramipril in Normotensive Patients.
Belluzzi F, Sernesi L, et al:
J Am Coll Cardiol 2009; 53 (January): 24-29

ACE inhibitors may have beneficial effects in patients with lone atrial fibrillation by decreasing the risk of AF relapse.

**Background**: Patients with atrial fibrillation (AF) frequently have negative structural and electrical remodeling. Angiotensin-II converting enzyme (ACE) inhibitors are known to decrease AF relapses in patients with structural heart disease and/or other comorbidities.

**Objectives**: To assess whether ACE inhibitors have protective effects against such remodeling in patients with lone AF and whether they can decrease the risk of future AF recurrence.

**Methods**: 62 patients with a first ever episode of AF in the absence of structural heart disease, systemic hypertension, or other causes of secondary AF (among other exclusions) were included. Duration of AF had to be <12 hours. Patients were pharmacologically cardioverted to sinus rhythm and then randomized to ramipril 5 mg daily or placebo. Baseline echocardiograms were performed on all patients. Patients were followed with Holter monitors and clinical examinations every 3 months for 3 years. Primary end point was the first recurrence of AF after cardioversion.

**Results**: There were 31 patients in each of the placebo and ramipril groups. There were no significant baseline demographic, echocardiographic, or serum chemistry differences between the 2 groups. The ramipril group had a minor but significant reduction in systolic blood pressure (BP) from 136 to 128 mm Hg. The placebo group had a minor, nonsignificant, increase in BP. Echocardiographic follow-up of the ramipril group demonstrated no significant change in chamber size compared to baseline. Patients in the placebo group had a small increase in the left atrial diameter and area. By the end of the study follow-up, there were 3 cases of AF relapses in the ramipril group compared to 10 such cases in the placebo group ($P<0.03$).

**Conclusion**: Ramipril, likely representing a class effect of ACE inhibitors, decreases incidence of AF relapses in patients with lone AF. The exact mechanism of the beneficial effect is not known and multiple mechanisms may play a role.

**Reviewer's Comments**: Lone AF is a less ominous disease than AF associated with structural heart disease or systemic hypertension. However, it still caries a sizable risk of thromboembolic events in addition to the potential of negatively affecting patients' quality of life. ACE inhibitors have been found in many previous studies to be effective in preventing negative remodeling in patients with AF with significant comorbidities. This current study seems to extend this beneficial effect to patients with lone AF. There is little downside to placing such patients on ACE inhibitors given their multiple beneficial effects. Nevertheless, the concepts presented here need to be further verified in larger studies to establish evidence-based guidelines. (Reviewer-Khalid Almuti, MD).

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Keywords: Angiotensin-II Converting Enzyme Inhibitors

Print Tag: Refer to original journal article
Significant Beneficial Effect of Vital Capacity Maneuver

Effects of Early Vital Capacity Maneuver on Respiratory Variables During Multivessel Off-Pump Coronary Artery Bypass Graft Surgery.
Shim JK, Chun DH, et al:

Crit Care Med 2009; 37 (February): 539-544

There is a significant beneficial effect of a vital capacity maneuver on shunt fraction and oxygenation as well as lung mechanics and time spent on mechanical ventilation.

**Objective:** To determine whether similar recruitment maneuvers could help off-pump cardiopulmonary bypass (OPCAB) patients.

**Participants/Methods:** Exclusion criteria for the study were left ventricular ejection fraction <40%, severe lung disease prior to surgery, a forced vital capacity <80% of predicted, abnormal arterial blood gases preoperatively, or the presence of renal, hepatic, or cerebrovascular disease. Standard techniques for monitoring the patients postoperatively were maintained for the entire study area. During surgery, patients were ventilated using a tidal volume of 7 to 8 mL/kg in an inspiratory/expiratory time ratio of 1:2. Patients were randomly allocated to either the vital capacity maneuver group or the control group. A reservoir bag was used to inflate the lungs to 40 cm of water pressure, and this was maintained for 10 seconds under direct visualization. This was applied from the time of surgery through the period until extubation was achieved. Shunt fraction was measured using standard techniques. Dynamic and static compliance were measured as was respiratory index. Decisions for extubation as well as discharge from the ICU were made by the ICU staff. Standard criteria for weaning the patient from mechanical ventilation were applied to both groups.

**Results:** 50 patients were successfully treated with OPCAB. There were no significant differences in the baseline pulmonary variables. Shunt fraction was significantly lower in the patients who received vital capacity maneuver when compared to controls at 6.5% versus 3.5%. PaO₂/FIO₂ was significantly higher in the vital capacity group as well. Pulmonary compliance was significantly better when compared to the control group. Hemodynamic variables, however, were similar in both groups, as were cardiac enzyme, fluid administration, urine output, blood loss, and the amount of units transfused; the use of suppressors was identical as well. The time to extubation was significantly shorter in the vital capacity group than in the control group.

**Conclusions:** There is a significant beneficial effect of vital capacity maneuver on shunt fraction and oxygenation as well as lung mechanics and time spent on mechanical ventilation.

**Reviewer's Comments:** This is a rather well-done study re-demonstrating the benefit of vital capacity maneuvers both in the pre-extubation period in the operating room and in the recovery room and ICU. There were significant improvements in lung mechanics, hemodynamics, and shunt fraction, all of which were accomplished with virtually no adverse reactions and virtually no additional cost to the patient. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Postoperative Respiratory Management

Print Tag: Refer to original journal article
Is Dopamine the Preferred Vasopressor for Septic Shock?

Influence of Vasopressor Agent in Septic Shock Mortality. Results From the Portuguese Community-Acquired Sepsis Study (SACiUCI Study).

Póvoa P, Carneiro AH, et al:

Crit Care Med 2009; 37 (February): 410-416

Patients with community-acquired septic shock have poor outcomes with norepinephrine when compared to dopamine.

**Objective:** To evaluate vasopressors in a group of patients who presented only with sepsis.  
**Design:** Prospective multicenter observational study performed in multiple different ICUs in Portugal.  
**Participants/Methods:** Standard definitions for infection were used. Community-acquired infection was defined as the onset of infection prior to or within the first 48 hours of arrival at the hospital. Standard definitions for severe sepsis and septic shock were used. Patients were categorized based on their primary diagnosis at admission and the source of sepsis. Data were extracted from the ICU charts by trained investigators.  
**Results:** 17 ICUs participated, and 4202 patients (with each case report form containing 237 items) were admitted to those ICUs during the study period; 60 patients were excluded resulting in 4142 patients to be analyzed (median age, 64 years). There was a preponderance of men (61%). Among the patients, 54% were medical noncoronary admissions, 4% were medical coronary, 13% were trauma, 15% were scheduled for surgery, and 14% for emergency surgery. Within the cohort, 22% of the patients admitted met the criteria for community-acquired sepsis. The demographic characteristics were similar to the group as a whole and the median Simplified Acute Physiology Score II score was 47. Approximately 61% of the patients had an infection in the lungs, followed by the abdomen and urinary tract. Cultures were positive in 40% of the patients. The overall ICU mortality rate was 30% and in-hospital mortality was 38%. Norepinephrine was the most frequently administered vasopressor at 73% followed by dopamine and then combined therapy. Patients who received levofed had a higher mortality rate (52%) when compared to patients who received dopamine alone (39%). Dobutamine patients had the highest mortality of all. Patients who received all 3 of vasopressors were excluded from analysis. Levofed and dobutamine were associated with an increased risk at 3.5 and 1.52, respectively.  
**Conclusions:** Patients with community-acquired septic shock have poor outcomes with norepinephrine when compared to dopamine.  
**Reviewer's Comments:** This study, although quite intriguing, has 1 serious flaw; it was not a randomized trial, and 73% of the patients received levofed as a single agent, with the remainder receiving other single agents or a combination of agents. It is quite possible that the physicians felt that the sickest patients would require levofed or that some of the characteristics of the patients would be better treated with this agent than with dopamine. (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: Septic Shock

Print Tag: Refer to original journal article
ODI May Be Useful in Characterizing Patients With OSAHS

Comparison of the Indices of Oxyhemoglobin Saturation by Pulse Oximetry in Obstructive Sleep Apnea Hypopnea Syndrome.

Lin C-L, Yeh C, et al:

Chest 2009; 136 (January): 86-93

For predicting the severity of OSAHS, the ODI clinically has the higher correlation with AHI than time-domain and frequency-domain indexes.

**Background:** Obstructive sleep apnea and hypopnea syndrome (OSAHS) is a common disease; polysomnography (PSG) is the current standard for a definitive diagnosis. However, PSG is expensive, time consuming, and labor intensive. Oxyhemoglobin indexes from pulse oximetry have been used to screen and predict sleep apnea-hypopnea severity. During apneic or hypopnea periods, airflow limitation may lead to recurrent episodes of hypoxemia that can be detected on oxyhemoglobin as fluctuations in oxyhemoglobin saturation by pulse oximetry. Three kinds of oxyhemoglobin indexes are available to measure this irregular fluctuation: the oxyhemoglobin desaturation index (ODI); the time-domain index; and the frequency-domain index proposed previously. There has been no systematic comparison of their relative utility in the diagnosis of OSAHS.

**Objective:** Researchers performed this study to comprehensively evaluate the ability and reliability of oxyhemoglobin indexes and to verify whether or not pulse oximetry can reduce sleep laboratory efforts to diagnose the severity of OSAHS, using an automated digital analysis.

**Participants/Methods:** Patients were recruited from the China Medical University Hospital Centre. All patients were diagnosed as OSAHS with polysomnography. There were 257 patients in the learning set and 279 patients in the validation set. Three kinds of oxyhemoglobin indexes, including the ODI, time-domain index, and frequency-domain index were used. Oximetry indexes first analyzed the accuracy and reliability of the detection of OSAHS. They calculated best standard error of estimate (SEE) between apnea-hypopnea index (AHI) and the ODI, time-domain index, and frequency-domain index. Then they analyzed the sensitivity and specificity of the diagnosis of moderate (AHI, ≥15/hour) and severe (AHI, ≥30/hour) OSAHS patients based on the best SEE.

**Results:** ODI had a better diagnostic performance than the time-domain and frequency-domain indexes. For predicting the severity of OSAHS, the ODI clinically had the higher correlation with AHI than time-domain and frequency-domain indexes.

**Reviewer’s Comments:** There are several limitations to this study. The selected OSAHS threshold for the subjects may have affected the sensitivity and specificity results. Oxyhemoglobin desaturation may not be seen in all of the respiratory events. In addition, oxyhemoglobin desaturation drops during the night were not always consistent with respiratory events. The oximetry signal alone is unable to determine whether the subject is sleeping or not. Also oximetry cannot detect other sleep-related disorders like restless legs syndrome and periodic leg movement disorder. The authors claim that the ODI index provided a high level of diagnostic sensitivity and specificity at different degrees of OSAHS severity. ODI index may be helpful for diagnosis of OSAHS, however, it is far from having the diagnostic value of PSG (Reviewer-Eric H. Gluck, MD, JD).

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Keywords: OSAHS

Print Tag: Refer to original journal article
Sodium, Potassium Intakes Affect Risk of CVD

Joint Effects of Sodium and Potassium Intake on Subsequent Cardiovascular Disease: The Trials of Hypertension Prevention Follow-Up Study.

Cook NR, Obarzanek E, et al:

Arch Intern Med 2009; 169 (January): 32-40

Increases in the sodium to potassium excretion ratio are associated with an increased risk of subsequent cardiovascular disease.

**Background:** Various prior studies of dose-response effects of sodium and potassium intake on subsequent cardiovascular disease (CVD) have relied on sub-optimal measures of intake. Prior observational data and randomized trials have shown decreased blood pressures and a reduced risk of hypertension in those subjects with increased potassium intake and decreased sodium intake.

**Methods:** There have been 2 trials of sodium reduction and other interventions that collected 24-hour urinary excretions intermittently during 18 months from September 17, 1987, to January 12, 1990 (Trials of Hypertension Prevention [TOHP] I) and during 36 months from December 18, 1990, to April 7, 1995 (TOHP II). These trials included adults with pre-hypertension aged 30 to 54 years. Amongst those adults not assigned to an active sodium reduction intervention, the relationship of a mean of 3 to 7 urinary excretions (24 hour) of sodium and potassium and their ratio with subsequent CVD (stroke, myocardial infarction, coronary revascularization, or CVD mortality) through 10 to 15 years of post-trial follow-up were assessed.

**Results:** Among 2974 participants follow-up information was obtained on 2275 participants. There were 193 CVD events. After adjustments for baseline variables and lifestyle changes, there was a non-significant trend in CVD risk across sex-specific quartiles of urinary sodium excretion (\(P = 0.38\) for trend) and potassium excretion (\(P = 0.08\) for trend). There was, however, a significant trend across quartiles of the sodium to potassium excretion ratio (\(P = 0.04\) for trend). In those models containing both measures simultaneously, linear effects were: rate ratio (RR), 1.42; 95% confidence interval (CI), 0.99 to 2.04 per 100 mmol/24 h of urinary sodium excretion (\(P = 0.05\)); and 0.67; 0.41 to 1.10 per 50 mmol/24 h of urinary potassium excretion (\(P = 0.12\)). A single model containing the sodium to potassium excretion ratio (RR, 1.24; 95% CI, 1.05 to 1.46; \(P = 0.01\)) had the lowest Bayes information criterion (best fit). **Conclusion:** Increased sodium to potassium excretion ratio is associated with increased risk of subsequent CVD. This effect is stronger than that of sodium or potassium individually.

**Reviewer's Comments:** This paper is important since it highlights the importance of dietary intake and subsequent risk of CVD. Current diets are rich in salt. Prior studies have illustrated a decrease in blood pressure in subjects with an increased potassium intake and decreased sodium intake. This study illustrates that higher sodium to potassium excretion ratio is associated with an increased risk of subsequent CVD. (Reviewer-Suraj Maraj, MD).

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Keywords: Cardiovascular Disease

Print Tag: Refer to original journal article
Determining the Better Therapy for AF Patients

Benefit of Oral Anticoagulant Over Antiplatelet Therapy in Atrial Fibrillation Depends on the Quality of International Normalized Ratio Control Achieved by Centers and Countries as Measured by Time in Therapeutic Range.

Connolly SJ, Pogue J, et al:

Circulation 2008; 118 (November): 2029-2037

The necessity of maintaining a therapeutic international normalized ratio cannot be overestimated when treating patients with atrial fibrillation.

Background: Patients with atrial fibrillation (AF) are at an increased risk of stroke and other vascular events. Oral anticoagulation (OAC) with warfarin has been shown to be superior to antiplatelet agents in the prevention of such events. An international normalized ratio (INR) in the range of 2 to 3 is the standard of care. Clinicians need to maximize their patients' time in therapeutic range (TTR) to provide them with maximum protection. Various studies have suggested that many patients spend a significant time outside that range. A low TTR has been associated with increased incidence of stroke.

Objective: To explore how variations in TTR between countries and centers affect the efficacy of OAC when compared with dual antiplatelet agents.

Methods: This was a post-hoc analysis of a subset of patients enrolled in a large study (ACTIVE W) of dual antiplatelet agents (aspirin and clopidogrel) compared to warfarin. All patients had AF with a ≥1 other risk factor for stroke. TTR was defined as percentage of days with INR of 2 to 3.

Results: 3371 patients in the OAC group were included in the current analysis. Mean TTR for all OAC patients was 63%. Patients were more likely to have a subtherapeutic rather than a supratherapeutic INR. There were considerable variations in mean TTR between the 29 participating countries (range 46% to 78%). In all, 15 countries with enough clinical events were included in analysis of OAC efficacy compared to dual antiplatelet agents. Patients were divided into quartiles based on their TTR. Relative risk of stroke or vascular events for the OAC and dual antiplatelet groups increased from the lowest to the highest quartiles. Patients in the 2 lowest TTR quartiles had more risk of such events with dual antiplatelet agents compared to warfarin. Conversely, patients in the 2 highest TTR quartiles had less risk of stroke with dual antiplatelet agents compared to warfarin. A similar outcome was noted for major hemorrhage. These effects were largely independent of baseline differences between the quartiles. More complex statistics were used to determine the minimum TTR that would be associated with benefit from OAC. That value was determined to be a TTR of 58%.

Conclusions: The success of INR control in the therapeutic range is an important determinant in achieving a benefit from OAC over antiplatelet agents. The study suggests that there is a TTR threshold (58%) below which OAC therapy may not be superior to antiplatelet therapy.

Reviewer's Comments: This study has serious implications for healthcare delivery systems. Simply placing patients on OAC is not sufficient to derive a benefit. Serious efforts must be directed at achieving and maintaining a therapeutic INR. (Reviewer-Khalid Almuti, MD).

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Keywords: Atrial Fibrillation

Print Tag: Refer to original journal article
Fish oil supplementation decreases CV mortality, but has no effect on arrhythmia.

**Background:** Over the last decade, there has been great interest in the possible cardioprotective effect of fish oil. The interest started in the mid 1970s when a study from Greenland showed that a diet high in fish oil was associated with low cardiovascular (CV) mortality. Other studies over the years, including the large GISSI-Prevenzione trial showed decreased CV mortality, sparking interest in the possibility that part of the CV protection was due to an antiarrhythmic property of fish oil.

**Objective:** To evaluate the literature on the effects of fish oil on mortality and arrhythmias.

**Methods:** Randomized controlled trials of fish oil supplementation were reviewed using the usual data sources available. The primary outcomes of interest were arrhythmic outcomes in patients with defibrillators and sudden cardiac death. The secondary outcomes were all-cause mortality and death from cardiac causes.

**Results:** 12 studies were included involving 32,779 patients. The studies did not show a decrease in arrhythmias, either in the 3 studies with implantable defibrillators or in the 6 studies for sudden cardiac death. A total of 11 studies looked at deaths from cardiac causes, with a significant decrease noted in cardiac deaths of 20%, (OR, 0.80; 0.69 to 0.92). There was no significant decrease in all-cause mortality.

**Conclusions:** Fish oil supplementation was associated with a significant reduction in deaths from cardiac causes, but there was no reduction in arrhythmias or all-cause mortality.

**Reviewer's Comments:** There have been many studies touting the benefits of fish oil. This analysis shows a small benefit in cardiac deaths, but no benefit in all-cause mortality or in the frequency of malignant arrhythmias. What should we advise our patients? If patients eat fish 2 or more times per week, they probably get no benefit from fish oil. If they do not eat fish, there is probably a small benefit to fish oil, but not on mortality. (Reviewer-Douglas S. Paauw, MD).

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Keywords: Arrhythmias

Print Tag: Refer to original journal article
Hand-held ultrasound is better than a cardiac physical examination by hospitalists at detecting cardiomegaly, pericardial effusions, and, to a lesser extent, left ventricular dysfunction.

**Background:** Diagnostic technologies such as echocardiography offer advantages in some settings over traditional physical examination. There is emerging literature on the utility of handheld ultrasound (HUS) units in cardiac examinations; HUS may duplicate some of the diagnostic utility of formal echocardiography.

**Objective:** To evaluate the accuracy of HUS in cardiac physical examinations performed by hospitalists on medical inpatients.

**Design:** This was a single-institution study performed over a 15-month period.

**Methods:** Eligible patients were admitted to the inpatient medical service and scheduled for a formal echocardiogram. Ten hospitalists received formal training in the use of SonoSite Elite HUS units and spent at least 6 hours reading echocardiograms with cardiologists. Hospitalists noted pericardial effusion and cardiomegaly, graded left ventricular systolic function, and noted valvular abnormalities (mitral regurgitation, aortic stenosis, or aortic regurgitation). Findings were graded on a 4-point scale: normal/no abnormality or mild, moderate, or severe abnormality. Prior to completing the HUS, hospitalists recorded their cardiac physical examination. The primary outcome was percentage of agreement between the physical examination and HUS, with echocardiography as a gold standard.

**Results:** The 10 hospitalists, with an average of 2.9 years (range, 0 to 9 years) of post-residency experience, completed 354 HUS procedures on patients admitted to the general medical service. The major finding of the study was that HUS improved the ability of hospitalists to detect pericardial effusion and cardiomegaly, and modestly improved the ability to detect left ventricular systolic dysfunction. Using HUS, the detection of pericardial effusion increased from 49% to 79% for exact matches, and from 59% to 96% for matches within one degree of accuracy (ie, mild vs moderate, or moderate vs severe). The detection of cardiomegaly improved from 59% to 90% with HUS. Measures of left ventricular function improved modestly from 46% to 59% for exact matches and from 67% to 88% for matches within one degree of accuracy. HUS did not substantially improve the accuracy of diagnosis of aortic stenosis, aortic regurgitation, or mitral regurgitation.

**Conclusions:** In the hands of hospitalists, HUS detected pericardial effusion, cardiomegaly, and the degree of left ventricular systolic dysfunction better than the physical examination; HUS did not substantially improve the accuracy of diagnosis of clinically important valvular disorders.

**Reviewer's Comments:** Like formal echocardiography, HUS may be a useful addition to the traditional cardiac physical examination. This study builds on previous reports that HUS adds to the physical examination performed by cardiologists, house staff, and medical students. HUS clearly does not supplant the value of formal echocardiography, particularly for valvular disorders. It also remains to be seen whether the information provided by HUS changes management. This is a crucial question, particularly given the significant expense of portable HUS units. (Reviewer-Paul R. Sutton, PhD, MD).

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Keywords: Physical Examination

Print Tag: Refer to original journal article
Can CT Coronary Angiography Replace Cardiac Catheterization?

Diagnostic Performance of Coronary Angiography by 64-Row CT.

Miller JM, Rochitte CE, et al:


CT coronary angiography can identify significant coronary stenoses in patients at high risk for heart disease, but it is falsely negative in 17% of patients.

Background: Given the high prevalence of coronary artery disease (CAD), there continues to be great interest in minimally invasive ways to evaluate for coronary stenoses. Currently, CT coronary angiography is being used with increasing frequency, but its sensitivity and specificity are still unclear.

Objective: To determine the accuracy of CT angiography as compared to conventional coronary angiography in patients at high risk for CAD.

Design: Prospective, multicenter, international diagnostic study.

Participants: To be eligible, patients had to be aged at least 40 years and be referred for coronary angiography for suspected symptomatic heart disease. Patients were not eligible if they had undergone cardiac surgery, had decreased renal function, or had elevated coronary calcium scoring (Agatston score >600).

Methods: Each patient underwent coronary calcium scoring and CT coronary angiography (with 64-row scanners) before also undergoing cardiac catheterization. For CT images, 2 independent observers quantitated the degree of stenosis, and a reading was performed with an available software program. Similar segments of artery were identified and measured with conventional coronary angiography. Obstructive lesions were considered clinically important if >50%.

Results: 291 patients were enrolled (median age, 59 years; 74% were male). The median time between CT study and conventional angiography was 10 hours. Overall, 56% of patients were found to have significant obstructive CAD. The sensitivity for CT angiography was 85% and specificity was 90%. For this population with a 56% prevalence, the positive-predictive value was 91% and the negative-predictive value was 83%. In a secondary analysis, CT angiography compared favorably with conventional angiography in predicting the need for coronary interventions. Only 2 patients had serious reactions to contrast dye, requiring hospitalization, and there were no cases of renal failure reported.

Conclusions: CT coronary angiography can identify significant coronary stenoses in patients at high risk for heart disease. However, 17% of patients with a negative study were found to have significant obstruction on conventional angiography, making it unlikely that CT has adequate accuracy to replace conventional angiography.

Reviewer’s Comments: The accompanying editorial offers strong words on the judicious (or lack thereof) use of new technologies, offering concern over the quick adaption and use of unproven diagnostic tests. At this point, the most clearly defined role for CT angiography has been to quickly "rule out" significant disease in lower-risk patients presenting with chest symptoms (partly as a way to avoid need for hospitalization). Now we have further information on patients at higher risk. Clearly, the test has the capacity to identify many patients with CAD. However, it remains unclear to me that it has any use in this high-risk population. (Reviewer-Mark E. Pasanen, MD).

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Keywords: Coronary Artery Disease

Print Tag: Refer to original journal article
Depression May Cause Cardiac Events Through Lack of Exercise

Depressive Symptoms, Health Behaviors, and Risk of Cardiovascular Events in Patients With Coronary Heart Disease.

Whooley MA, de Jonge P, et al:

JAMA 2008; 300 (November 26): 2379-2388

Physical inactivity may account for increased cardiovascular risk in patients with depression.

**Background:** Depression is a primary risk factor for the development of cardiovascular disease and is a marker of poor outcomes in those with established heart disease. The mechanism by which depression increases risk is unknown.

**Objective:** To determine the factors by which depression increases cardiovascular risk.

**Design:** Prospective cohort study.

**Methods:** The Heart and Soul Study enrolled patients with stable coronary artery disease from 12 outpatient clinics in San Francisco. Patients underwent screening examinations including behavioral assessment, psychiatric evaluation, laboratory tests, echocardiography, 24-hour electrocardiography, and a treadmill test. The Patient Health Questionnaire was used to measure depressive symptoms. Participants were interviewed on a yearly basis, and events were confirmed by a review of the medical records. The primary outcomes were heart failure, transient ischemic attack, stroke, myocardial infarction, and/or death.

**Results:** Of 1024 patients enrolled in the study, 199 (19.6%) had baseline depression. Patients with depression were significantly more likely to smoke, be younger (63 vs 68 years), be less active, be heavier, be less compliant with medications, be on more antidepressants, and have more comorbid conditions. Average follow-up was 4.8 years, and there were 341 cardiovascular events. The age-adjusted annual rate of events was higher in patients with depression (10%) than in those without (6.7%; HR, 1.5; 95% CI, 1.16 to 1.95). In multivariate analysis, depression continued to be associated with a 31% increase in events. This increased risk for any cardiac event in patients with depression was nullified when adjusted for physical inactivity.

**Conclusions:** The association between depression and cardiovascular events may be largely explained by modifiable behaviors such as physical inactivity.

**Reviewer's Comments:** This study reinforces the association between depression and poor outcomes from other chronic medical conditions. Encouraging exercise in all patients is important. Physical exercise in patients with depression may help improve their depressive symptoms and lower their risk of cardiovascular events. (Reviewer-Deborah L. Greenberg, MD).

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Keywords: Cardiac Effects

Print Tag: Refer to original journal article