Elevated CRP linked to standard heart disease risk factors

Elevated C-reactive protein (CRP) levels are usually accompanied by high cholesterol levels and other coronary heart disease (CHD) risk factors, according to data from the Third National Health and Nutrition Examination Survey (NHANES).

Moreover, CRP elevation is rare in the absence of borderline or abnormal risk factors. Michael Miller from the University of Maryland, Baltimore states that although CRP is an excellent barometer of inflammation, it simply reflects a hostile environment induced by inactivity, central weight gain, smoking and other heart disease promoting risk factors.

An analysis of 15,341 participants demonstrated the relationship of CHD risk factors and CRP beyond 3 mg/L. In weighted multivariate logistic regression analysis, a high CRP was significantly more common with obesity, overweight, and diabetes.

High CRP was rare in the absence of any borderline or abnormal CHD risk factor in men (4.4%) and women (10.3%). Overall, however, the risk of elevated CRP level attributable to the presence of any abnormal or borderline CHD risk factor was 78% in men and 67% in women. Thus the researchers conclude that CRP measurement may have limited utility as a screening tool beyond other known CHD risk factors.

In an accompanying editorial, Russell P. Tracy and Lewis H. Kuller from the University of Vermont in Burlington agree and note that this position is consistent with the Centres for Disease Control and Prevention and American Heart Association guidelines.

Source: Arch Intern Med 2005;165:2058-2060,2063-2068

Restless legs syndrome common in diabetes

Restless legs syndrome (RLS) is common in patients with type 2 diabetes. Restless legs syndrome can be a major cause of sleep disruption in this population. Veralice M. S. de Bruin et al from Brazil, examined the presence of RLS and the quality of sleep in patients with type 2 diabetes. Included in the cross-sectional study were 100 consecutive patients who regularly attended a diabetes clinic at the University Hospital.

The study used the Pittsburgh Sleep Quality Index to assess the patients’ quality of sleep and the Epworth Sleepiness Scale to measure excessive daytime sleepiness. The four minimum criteria defined by the International Restless Legs Syndrome Study Group were used to diagnose RLS.

RLS was detected in 27 patients, 25 of whom had peripheral neuropathy. An association between RLS and peripheral neuropathy was confirmed by logistic regression analysis (p = 0.001).

Overall, 45% of the patients had poor sleep quality, which was associated with age, the presence of RLS and peripheral neuropathy. Twenty-six percent of subjects exhibited excessive daytime sleepiness, which was not associated with the presence of RLS. Based on these findings, it was suggested that people with type 2 diabetes be screened for RLS, especially patients with polyneuropathy.


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Regular exercise may help suppress inflammation in healthy adults

Exercise training markedly lowers plasma C-reactive protein (CRP) levels in healthy sedentary adults with high levels of this inflammatory marker.

The possible inflammation suppressing effect of exercise training may partly explain the effectiveness of regular physical activity in the prevention and treatment of cardiovascular and metabolic diseases. Timo A. Lakka from the University of Kuopio et al had 652 healthy white and black men and women who had not participated in regular physical activity over the prior 6 months take part in a 20-week standardized exercise-training program. They trained three times per week at a level of 75% of baseline VO2-max.

At baseline, 265 subjects had low CRP levels (< 1.0 mg/L); 225 had moderate CRP levels (1.0 to 3.0 mg/L); and 162 had high CRP levels (> 3.0 mg/L).

The principal finding in this study is that plasma CRP fell by about 1.3 mg/L (or 24%) in response to 20 weeks of regular exercise in individuals with high baseline CRP levels. The reduction in CRP was consistent across all population groups and varied between 1.2 and 2.2 mg/L. This observation is potentially important from a public health and clinical point of view. Individuals with high CRP levels make up about one-fourth of the adult population and have a markedly increased risk of type 2 diabetes and cardiovascular disease.

A CRP reduction of 1-2 mg/L can significantly decrease the risk of cardiovascular diseases and type 2 diabetes in individuals who have high CRP levels. In this study, CRP levels did not change in response to exercise in individuals with low or moderate baseline CRP levels.

In a related commentary, Joep Perk from Oskarshamn, Sweden suggests that for individuals at increased risk for cardiovascular disease, elevated CRP may become a prognostic tool for cardiologists and general practitioners: it may identify those for whom exercise training will be effective.


Weight loss surgery helps prevent diabetes in morbidly obese patients

The long-lasting weight loss achieved with laparoscopic gastric banding can help in the prevention and remission of type 2 diabetes in morbidly obese patients, according to a report in the November issue of Diabetes Care. The surgery also helps stave off hypertension.

The findings are based on a study of 73 morbidly obese patients who underwent laparoscopic adjustable gastric banding (LAGB) and 49 comparison subjects who refused the surgery. Separate studies were conducted to assess the effect on diabetes prevention and on remission.

At the end of the 4-year follow-up, Antonio E. Pontiroli, from Ospedale San Paolo in Milan, Italy, and colleagues found that LAGB-treated patients experienced a drop in BMI from 45.9 to 37.7, whereas control subjects experienced no significant change.

In the prevention arm, five of the control subjects (17.2%), but none of those treated with LAGB developed type 2 diabetes during follow-up (p = 0.0001). In the remission arm, one control subject (4.0%) and seven LAGB-treated subjects (45%) went into diabetes remission (p = 0.0052).

LAGB also had a beneficial effect on hypertension. Just one LAGB-treated patient developed this problem compared with 11 control subjects. In addition, hypertension resolved in 15 LAGB patients and in one control (p = 0.0001 for both).

These data suggest that LAGB is effective in preventing and promoting the remission of established type 2 diabetes and arterial hypertension.

Longitudinal changes in HbA1c reflect quality of diabetes care

Quality of diabetes care can be assessed by measuring longitudinal changes in HbA1c, according to a report in the issue of Health Services Research. "Longitudinal methods like those we used in our study represent a different kind of information than currently monitored for quality of healthcare," Monika M. Safford from University of Alabama at Birmingham said. "This is more of a 'movie' than the currently widely used 'snapshot.'"

Safford et al investigated the feasibility of using within-patient longitudinal changes in HbA1c as an alternative to cross-sectional measures of quality of diabetes care in 125 VA facilities nationwide. In two different statistical models, most VA hospitals showed downward trends in within-patient HbA1c curves over time. Only 20 facilities had monthly rises in HbA1c, and for all but 5, the 95% confidence interval of the slopes included zero. The researchers were also able to use these curves to rank 105 facilities, thereby allowing an assessment of comparative performance with a selected confidence interval. There remained, however, considerable uncertainty in the rankings. The longitudinal approach presented here measures changes in HbA1c over time within individuals, effectively overcoming some of the cross-sectional problems and capturing a new domain in quality measurement.

"We suggest evaluation and comparison of these within-patient change rates may prove to be a useful new approach to studying the quality of ongoing care to a population with chronic disease and may identify those facilities that could be more closely evaluated for best (and more problematic) practices," the authors conclude.

"Because this is a new approach in this field, like all new research, it should be confirmed prior to implementation," Safford added. "Nevertheless, longitudinal methods are likely to be taken up in some form as the quality-of-healthcare field continues to evolve."

Source: Health Services Research 2005;40:1818-1835

Glucose modulates food intake in patients with diabetes

Results of a study published in Diabetes Care suggest that glucose has an inhibitory influence on food intake in patients with type 2 diabetes.

"A gain in body weight is a common adverse effect of glucose-lowering therapies in patients with type 2 diabetes, the mechanisms of which are not completely understood," Bernd Schultes et al from the University of Luebeck, Germany, write. "Blood glucose is considered to play a crucial role in the regulation of food intake."

They examined the hypothesis that a short-term reduction of blood glucose concentration to normal values would acutely increase food intake in patients with type 2 diabetes. In a single-blind study, 12 diabetic patients were examined twice, once during a euglycaemic (5.0 mmol/L) clamp experiment and once during a hyperglycaemic (10.5 mmol/L) clamp.

Insulin was infused in both clamp conditions at a constant rate of 2.5 mU/kg per min for 125 minutes. A glucose solution was infused simultaneously at a variable rate to achieve target glucose levels. The patients were allowed to eat as much as they wanted from a standard breakfast buffet, during the last 30 minutes of the clamps.

Patients ingested an average of 25% more energy during the euglycaemic clamp than during the hyperglycaemic clamp (645 versus 483 kcal) and ate significantly more carbohydrates, proteins and fat.

However, when the total influx of energy was calculated, by adding the energy ingested by food and infused by glucose, this was almost identical for the euglycaemic and hyperglycaemic conditions (794 versus 790 kcal).

Thus, the researchers conclude, "total energy supply to the organism is tightly regulated on a short-term basis independent of the route of influx."

Source: Diabetes Care 2005;28:2884-2889
When starting patients on statin therapy, it’s important to acquaint them with the characteristic ways in which statin-associated myopathy differs from everyday aches and pains, Robert A. Vogel said. Statins, he stressed, comprise a “tremendously safe class of drugs.” The most feared complication – rhabdomyolysis – is rare. A great many patients inappropriately stop taking their medication because they over-interpret the significance of their aches and pains, said Vogel, professor of medicine and director of clinical vascular biology at the University of Maryland, Baltimore.

Statin-associated myopathy involves symmetric large-muscle pain, usually associated with tenderness upon squeezing. It is often accompanied by weakness. In fact, in older patients muscle weakness very often predominates over pain. “I tell patients it feels like the flu. You’re sore all over. You’re weak. And I think it’s very helpful to measure creatine kinase at the time you write a prescription for a statin. I tell the patient that if you get symmetric big-muscle pain and weakness, go to the lab and get this test done. Four hours later I can get the CK, and we know what we’re dealing with.”

The distinction between statin-associated myalgia and myositis is crucial. In myalgia, which is a benign, the serum CK level is within the normal range. Management involves reassurance, a change of statin, a lower dose, or 30 mg/day of coenzyme Q10, which Vogel has found works well in many of his patients.

In contrast, statin-associated myositis as defined by a CK level greater than 10 times the upper limit of normal dictates that statins be discontinued altogether.

However, statin-associated myositis with histologic muscle damage despite a normal CK result has been described (Ann. Intern. Med. 2002;137:581-5). This condition is thought to be rare and usually is linked with objective signs of muscle weakness.

Until Vogel began issuing CK lab slips when prescribing a statin, he found many of his patients who developed muscle soreness simply quit taking their medication and didn’t inform him until they came in several months later. By then it was be impossible to determine whether they had had myalgia or myositis because a statin-related elevated CK would have returned to normal.

Benign statin-associated myalgias are common. In the landmark 10,001-patient Treating to New Targets (TNT) trial, myalgia occurred in 4.8% of patients randomised to atorvastatin at 80 mg/day and 4.7% on 10 mg/day. And therein lies an important lesson. By dosing up, which is often required to get patients to goal, we are not costing our patients more muscle pain. That is a key concept for consideration because patients are not ‘safer’ by keeping the dose of statins low,” Vogel stressed.

In the Collaborative Atorvastatin Diabetes Study (CARDs), the incidence of myositis was 0.1% with atorvastatin at 10 mg/day and 0.7% with placebo. The complication of statin therapy every physician justifiably fears is rhabdomyolysis. It is marked by muscle symptoms accompanied by a greatly elevated CK – up to 300,000 IU/L, along with elevated creatine and myoglobinaemia. Rhabdomyolysis carries a 4% mortality.

But rhabdomyolysis is exceedingly rare. A U.S. FDA study of more than 250,000 statin users concluded that a physician with 2,000 patients on either of the two most widely prescribed statins – atorvastatin and simvastatin – for 20 years will encounter, on average, one case of rhabdomyolysis.

Source: JAMA 2004; 292:2585-90