

High Body Mass Index Linked To Chronic Kidney Disease, Too

BY MIRIAM E. TUCKER
Senior Writer

WASHINGTON — Add chronic kidney disease to the list of problems linked with obesity.

That's the conclusion from data presented by Rebecca P. Gelber, M.D., at a conference on cardiovascular disease epidemiology and prevention sponsored by the American Heart Association.

Diabetes and hypertension, as well as increasing age, have been established previously as risk factors for chronic kidney disease, whereas obesity

is a primary risk factor for both diabetes and hypertension. But new data from the prospective Physicians' Health Study are the first to independently link body mass index (BMI) with the development of chronic kidney disease, said Dr. Gelber of Harvard Medical School and the Massachusetts Veterans Epidemiology Research and Information Center, Boston.

Blood samples were available at 14-year follow-up for 11,104

initially healthy male study participants (mean age 53 years). At baseline, about 38% of the subjects were overweight (BMI of 25-29.9 kg/m²) and 4% were obese (BMI of 30 or greater).

As expected, the overweight and obese men were more likely during the study period to have hypertension, diabetes, or cardiovascular events. They were also more likely to



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DR. GELBER

smoke, reported less alcohol consumption, were less physically active, and were more likely to report a family history of MI.

At follow-up, chronic kidney disease—defined as an estimated glomerular filtration rate (GFR) of less than 60 mL/min per 1.73 m²—had developed in 12% (1,377 men).

Higher baseline BMI was consistently associated with increased risk for chronic kidney disease. Compared with par-

ticipants in the lowest quintile of BMI (less than 22.7), the odds ratio for those in the highest quintile (greater than 26.6) was 1.42.

After adjustment for potential baseline confounders (age, alcohol consumption, exercise, smoking, and parental history of MI) as well as potential mediators of the association between BMI and chronic kidney disease (hypertension, diabetes, cholesterol, and cardiovascular disease), the relationship was attenuated but still significant, with an odds ratio of 1.24, Dr. Gelber reported at the meeting, also sponsored by the National Heart, Lung, and Blood Institute.

The association between BMI and chronic kidney disease remained significant, to a similar degree, when subjects were divided into normal, overweight, and obese BMI categories, when the definition of chronic kidney disease was narrowed to GFR less than 50, and when the men who were obese at baseline were excluded.

These findings support previous data suggesting that similar predisposing factors underlie both chronic kidney disease and CVD, Dr. Gelber noted. ■

Consider Renal Effects Of High-Protein Diets

BY KERRI WACHTER
Senior Writer

WASHINGTON — The renal effects of high-protein diets pose a strong risk of harm in patients with chronic kidney disease, Alton Friedman, M.D., said at a meeting sponsored by the National Kidney Foundation.

Chronic kidney disease is often silent, so he recommends obtaining a serum creatinine measurement and a urinary dipstick test for proteinuria in all patients considering a high-protein diet for weight loss.

Those with a glomerular filtration rate of less than 60 mL/min should be advised against a high-protein diet, noted Dr. Friedman of Indiana University in Indianapolis.

Regardless of kidney function, protein intake increases glomerular filtration rate and renal blood flow by as much as 100% from baseline.

Over time, a high-protein diet appears to increase kidney volume and weight.

Studies suggest that high-protein diets increase urinary protein excretion in people with normal and in those with diminished kidney function, Dr. Friedman said.

High-protein diets are intend-

ed to induce ketosis by limiting carbohydrate intake. Increased ketone levels lead to increased sodium output, which in turn induces natriuresis, he said.

In the short-term, high protein consumption has been associated with orthostatic hypotension. There is little evidence that high-protein diets maintained for months adversely affect blood pressure, compared with standard low-fat diets.

Animal and human studies have shown that increased protein consumption leads to hyperuricosuria, hypercalciuria, hypocitraturia, and a reduction in urinary pH—all risk factors for the formation of kidney stones.

Healthy patients considering a high-protein diet should be advised about the potentially deleterious effects: chronic glomerular hyperfiltration and hyperemia, increased proteinuria, and an elevated risk for nephrolithiasis, Dr. Friedman said.

It may be helpful, he added, to point out to patients that although short-term studies (3-6 months) have resulted in more weight loss for high-protein diets than for standard diets, long-term studies (up to 1 year) have shown no differences in weight loss between the two groups.

Childhood Obstructive Sleep Apnea May Impair Memory and IQ

BY BETSY BATES
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RANCHO MIRAGE, CALIF. — Obstructive sleep apnea in children is associated with profound deficits in IQ, verbal comprehension, perceptual reasoning, and working memory, according to preliminary results of a case-control study at the Pediatric Sleep Disorders Center of Johns Hopkins University, Baltimore.

Ann C. Halbower, M.D., medical director of the center, reported that extensive cognitive deficits and cerebral metabolite alterations were powerfully evident in children from inner city Baltimore who suffered from moderate to severe obstructive sleep apnea (OSA).

Thus far, 17 children aged 7-16 years with OSA and 10 matched controls have completed sleep studies, neuropsychological tests, and magnetic resonance spectroscopy. The average age in both groups is 10.

"Our kids with OSA were severely impacted, their IQ scores being 10 to 15 or more points below normal. We saw huge differences in memory, especially in visual spatial processing, which is a parietal lobe function that has not received a lot of press," Dr. Halbower said at a conference on sleep in infancy and childhood spon-

sored by the Annenberg Center for Health Sciences.

Group differences in IQ were mostly explained by sharply defined deficits in working memory, nonverbal reasoning, and verbal comprehension among children with OSA.

Magnetic resonance spectroscopy determined that neuropsychological deficits in the children correlated with hippocampal metabolite alterations, low oxygen saturation, and body mass index (BMI).

The study is ongoing, although Dr. Halbower said she and her team are having trouble finding normal, nonsnoring obese controls who do not have sleep apnea. The average BMI among children with OSA was 29 and among controls, 19. African American children whose mothers completed about 12-14 years of education comprise the majority of the study cohort.

Subjects in the control group had significantly higher IQs than did those with OSA, but still not as high as controls enrolled in previous studies of sleep apnea. The mean full-scale IQ among controls was 101, and among children with OSA, 86.

Children with an IQ below 75, a history of seizures or depression, or use of psychotropic medications were not enrolled.

Intriguingly, some of the neuropsychological

functions most impacted by sleep apnea in adults were not significantly impaired in children with OSA. These included certain executive functions such as problem solving, planning, inhibitory control, sustained attention, and response preparation. Motor speed and cerebellar perceptual/motor timing appeared unaffected as well.

When respiratory parameters were assessed, children with OSA had a mean oxygen desaturation time at less than 95% of 70 minutes, compared with 0 for controls. To capture small, brief, intermediate hypoxic events, the oxygen saturation nadir also was studied, and was 75 for children with OSA and 93 for controls, a statistical difference with a significance of 0.0002.

The apnea/hypopnea index showed that children in the study had severe OSA, with a mean score of 29.1, compared with 0.3 for controls.

Researchers conducted two forms of magnetic resonance spectroscopy to attempt to pinpoint any cerebral metabolite changes that might be correlated with respiratory parameters and neuropsychological test results. A global brain assessment was conducted with general magnetic resonance spectroscopy imaging (MRSI) and a single voxel image was used to explore

metabolites within the anterior hippocampus on the left side.

Just six children with OSA and six controls have completed these studies.

However, preliminary results identified a "very significant" decline in *N*-acetyl aspartate/choline (NAA/Cho) ratios and choline/creatine (Cho/Cr) ratios in the hippocampal regions of children with OSA, compared with controls.

Both oxygen saturation nadir and oxygen saturation time at less than 95% correlated with brain metabolite dysfunction, IQ deficits, and BMI.

The apnea/hypopnea index correlated with brain metabolite problems, IQ problems, parietal lobe function problems, and BMI; however, the arousal and awake index failed to correlate with brain metabolite dysfunction, IQ, or BMI, "indicating that hypoxemia may be involved in the mechanism of these alterations," said Dr. Halbower.

Of interest, high BMI correlated with IQ deficits and low neuropsychological scores, but not with brain metabolites. The issue deserves further study, she said.

More subjects are being enrolled in the current investigation and researchers also are exploring possible reversibility of neurologic deficits with treatment of OSA. ■