Obesity suppresses cellular process critical to kidney health

October 5 2013

Obesity increases a chronic kidney disease patient's risk of developing kidney failure.

Obesity suppresses an important cellular process that prevents kidney cell damage, according to a study appearing in an upcoming issue of the *Journal of the American Society of Nephrology* (*JASN*). The findings suggest that restoring the process could protect the kidney health of obese individuals.

Obesity increases a chronic kidney disease patient's risk of developing kidney failure, but the mechanism underlying this connection has remained unclear.

Kosuke Yamahara, Takashi Uzu, MD, PhD (Shiga University of Medical Science, in Japan), and their colleagues suspected that decreased functioning of a process called autophagy might play a role. Autophagy is a degradation system within cells that removes damaged proteins and other defective cellular components, and autophagy insufficiency is common in obese individuals.

The researchers found that in normal-weight mice with kidney disease, autophagy was active in kidney cells. However, in obese mice with kidney disease, autophagy was suppressed and kidney cells became damaged. Normal-weight mice with kidney disease and defective autophagy (due to a gene deletion) also experienced kidney cell damage.

The investigators also discovered that a potent suppressor of autophagy (called mTOR) was hyperactivated in the kidneys of obese mice, and treatment with an mTOR inhibitor ameliorated autophagy insufficiency. Furthermore, both mTOR hyperactivation and autophagy suppression were observed in kidney specimens from obese patients with kidney disease.

"Obesity suppresses autophagy via an abnormal activation of nutrition sensing signals in the kidney," said Yamahara. "Our results suggest that restoring the kidney-protective action of autophagy may improve the kidney health of obese patients."

In an accompanying editorial, Ken Inoki, PhD (University of Michigan) stated that "the results of this study provide an important pathomechanism underlying obesity-associated renal… cell damage."

More information: The article, entitled "Obesity-mediated Autophagy Insufficiency Exacerbates Proteinuria-induced Tubulointerstitial Lesions," will appear online on October 3, 2013, DOI: 10.1681/ASN.2012111080

The editorial, entitled "Proximal Tubules Forget 'Self-Eating' When They Meet Western Meals," will appear online on October 3, 2013, DOI: 10.1681/ASN.2013070794

Provided by American Society of Nephrology