MedicalXpress

Researchers identify genetic factors linked to acquired narrowing of the airway

November 22 2017

Endotracheal intubation, in which a tube is inserted through the voice box (larynx) into the windpipe, and tracheotomy, in which surgery is undertaken to create a hole through the neck and into the windpipe (trachea) to facilitate breathing, are widely used in the hospital setting for elective surgery and in cases of serious illness or critical injury. In rare instances, however, the procedures result in the development of scarring and narrowing of the larynx and trachea, a condition known as acquired laryngotracheal stenosis (ALTS). Who is susceptible to ALTS - and why - is unclear, but according to new research at the Lewis Katz School of Medicine (LKSOM) at Temple University, genetic and ethnic background may be underlying factors.

"Many efforts have been made to decrease the risk of laryngeal and tracheal scarring through improved materials and techniques," explained Ahmed M.S. Soliman, MD, Professor and Interim Chair of Otolaryngology - Head and Neck Surgery; Director of the Voice, Airway, and Swallowing Center at LKSOM; and senior investigator on the new study. "Still, some patients develop ALTS, and now we realize that genetic differences, specifically those occurring in certain wound-healing genes, may put some patients at greater risk." The new study was published November 22 in the journal *Laryngoscope*.

ALTS affects an estimated one to eight percent of patients who have an endotracheal or tracheotomy tube placed. While the condition is rarely fatal, patients can develop difficulty breathing, necessitating complex emergency surgery to open the airway. It can also lead to voice and

swallowing dysfunction. In some cases, patients require permanent tracheotomy.

"Our hypothesis was that aberrations in wound healing, which are observed in patients with other scarring disorders, are related to ALTS," Dr. Soliman said. Knowing this, Dr. Soliman and colleagues decided to search the DNA of ALTS patients for specific changes in genes associated with scarring and wound healing.

A total of 138 patients were recruited from Temple University Hospital and its associated clinics for the study. Fifty-three of the recruits had ALTS, while the remainder of the patients were controls, individuals who had undergone endotracheal intubation or tracheotomy without scarring. DNA was isolated from each patient's blood and analyzed for the presence of any of six candidate genetic variations in a panel of scar formation and wound-healing genes.

Although none of the overall candidate variations was significantly associated with ALTS, when Dr. Soliman and colleagues carried out subgroup analyses, they found that certain variants were in fact significantly linked to ALTS, depending on ethnic background. The association with stenosis was high particularly for African Americans.

While the findings are preliminary, they pave the way for someday preventing ALTS through genetic testing. "If we know someone is at risk for developing ALTS, we could use alternatives to breathing tubes or use the tubes for only a short period of time, decreasing the chance of scar formation," Dr. Soliman said.

In the near-term, the next step is to confirm the new findings in a larger study, involving about 300 study patients. A multi-institutional trial would likely be needed to obtain this number. Such a large pool of patient data would greatly facilitate research on ALTS and open new

avenues of study into genetic aspects of other forms of laryngotracheal stenosis.

"We are particularly interested in using the techniques that we developed to study the genetics of idiopathic stenosis, which has no known cause," Dr. Soliman explained. "The idiopathic condition occurs almost exclusively in women of Northern European descent, suggesting the existence of additional associations between laryngotracheal stenosis and genetic and ethnic background."

Provided by Temple University