Clonal hematopoiesis is a phenomenon caused by mutations in hematopoietic stem cells and can lead to blood cancer. We now know that it occurs also in people with normal blood counts, where it is
associated with an increased risk of life-threatening atherosclerotic cardiovascular disease.

A research team at the Medical University of Vienna has now developed a genetic testing procedure to detect clonal hematopoiesis, which, when used in combination with an ultrasound examination of the carotid artery, allows to identify patients at high cardiovascular risk. The study was published in the *Journal of the American College of Cardiology*.

One of the most aspiring topics in cardiovascular research is the role of clonal hematopoiesis in cardiovascular disease. Recent work has shown that clonal hematopoiesis is frequent in the population with increasing prevalence at advanced age, detectable in up to 15% of individuals over the age of 70.

It may lead to malignant blood diseases, but most crucially greatly reduces life expectancy by increasing the risk for atherosclerotic cardiovascular disease. At an advanced stage, atherosclerosis can lead to the blockage of arterial blood vessels, thereby causing heart attacks and strokes.

An interdisciplinary team at MedUni Vienna led by Christoph Binder, Robert Kralovics and Roland Jäger from the Clinical Institute of Laboratory Medicine and Matthias Hoke from the Department of Internal Medicine II has now investigated the potential effects of clonal hematopoiesis on patients with proven, but asymptomatic carotid stenosis (atherosclerotic narrowing of the carotid artery).

For this, a novel assay based on high-throughput DNA sequencing was developed to perform targeted genetic testing, in order to identify causative mutations. This method was applied to approximately 1,000 blood samples derived from the ICARAS study (Inflammation and Carotid Artery-Risk for Atherosclerosis Study).
ICARAS represents a prospective cohort study that has been carried out at the Division of Angiology at the Department of Internal Medicine II since 2002, aiming at the identification of risk factors for atherosclerosis and cardiovascular endpoints such as myocardial infarction, stroke and cardiovascular death.

**Detection of increased risk before the appearance of symptoms**

The current study describes sharply increased mortality in patients with simultaneous carotid stenosis and clonal hematopoiesis. "The targeted design of the genetic testing procedure enabled us to reliably identify patients affected by clonal hematopoiesis," says lead author Roland Jäger.

With the joint detection of clonal hematopoiesis and carotid atherosclerosis, it was possible to discover a combined biomarker that can contribute to a personalized cardiovascular risk profile. High-risk patients can now be identified at an early stage, allowing for adequate adaptation of therapies and prevention of atherosclerotic disease progression, thereby reducing the risk for strokes and heart attacks.

"With the help of ultrasound-based duplex sonography in combination with the new genetic testing procedure, elevated cardiovascular risk can be detected long before the appearance of disease symptoms," explains co-lead author Matthias Hoke.

The corresponding authors of the study, Christoph Binder and Robert Kralovics, emphasize that "the results of this study provide the basis for future studies to investigate the role of clonal hematopoiesis in cardiovascular diseases," with the aim to implement this type of genetic diagnostics in laboratory medicine.

Provided by Medical University of Vienna


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