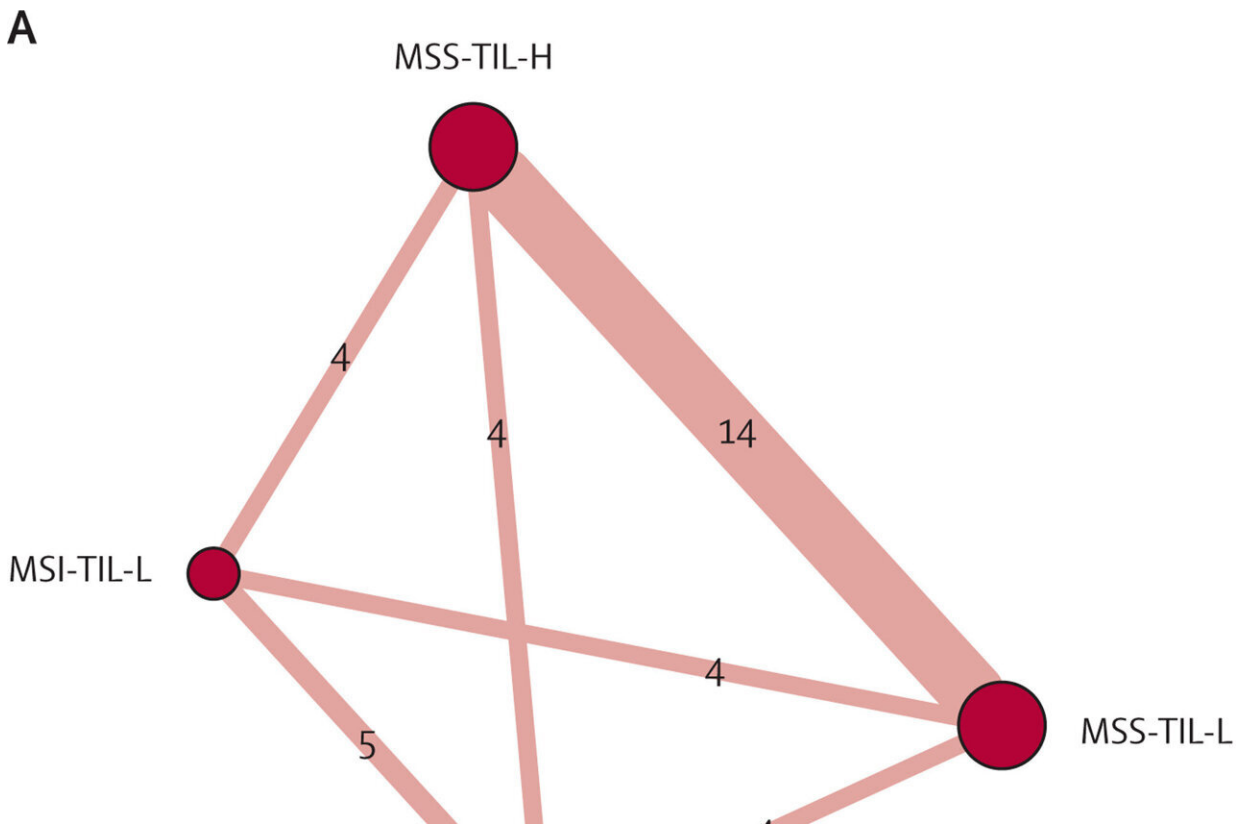
Combining two tumor markers can help track down colorectal cancer subtypes

May 16 2024



Disease-free survival. Credit: *The Lancet Gastroenterology & Hepatology* (2024).
DOI: 10.1016/S2468-1253(24)00091-8

Colorectal cancer differs from patient to patient. That is why scientists are looking for characteristic tumor markers that allow them to make

predictions about the likely response to certain therapies and the individual prognosis. The aim is to identify colorectal cancer subtypes so that these can then be treated in a customized manner. Two informative markers are microsatellite instability (MSI) and tumor-infiltrating lymphocytes (TIL). As researchers at the German Cancer Research Center (DKFZ) have shown, it makes sense to combine the two markers.

"MSI and TIL are established biomarkers in colorectal cancer. The question is: is it possible to make even more differentiated predictions by combining the two markers? We investigated this question by combining all available studies and evaluating them together.

"The result of this meta-analysis suggests that a classification system that records MSI and TIL together is suitable for optimizing the prognostic assessment of early-stage colorectal cancer," says DKFZ researcher Michael Hoffmeister, last author of the meta-analysis.

Microsatellite instability—what does that mean? Microsatellites are short DNA sequences in the genome that are repeated hundreds of times and are particularly susceptible to errors when copying genetic information. The cells can repair such mismatch errors. However, if the repair system does not function properly, mismatch errors accumulate and the length of the microsatellites changes. This is known as microsatellite instability (MSI).

In colorectal cancer, testing the tumor tissue for MSI is informative because tumors in early stages (without metastases) with high microsatellite instability (MSI-H) have a better prognosis than colorectal cancer with microsatellite stability (MSS). This is important for therapy planning.

In particular, MSI-H tumors can be treated well with modern immunotherapeutics—so-called checkpoint inhibitors—while MSS

tumors respond less well to these drugs. On the other hand, there are also therapies that have been shown to have little effect on MSI tumors. Testing for MSI is therefore now routinely used in colorectal cancer in order to find the best possible therapy for the individual patient.

According to first author Durgesh Wankhede, the meta-analysis now presented argues in favor of further differentiating the MSI subtype depending on whether lymphocytes have migrated into the tumor tissue or not. Lymphocytes are immune cells that play a central role in the defense against cancer. The presence of immune cells in tumor tissue has—as expected—proven to be prognostically favorable.

"We now wanted to know whether we would gain additional information by combining MSI and TIL. There are already a number of studies that have investigated this question, but the significance of these trials was limited, mainly due to the small number of cases. We therefore combined 21 studies with a total of around 14,000 patients and were able to differentiate between four subtypes with different prognoses based on this extensive data material," explains Hoffmeister.

Colorectal cancer patients whose tumors had a high microsatellite instability and a high number of infiltrating lymphocytes (MSI/TIL-H) had the best prognosis. Patients with this marker combination lived longer overall, and they lived longer disease-free. Microsatellite stability plus lymphocyte infiltration (MSS/TIL-H) proved to be the second most favorable constellation.

In contrast, patients with little or no immune cells found in the tumor tissue had a comparatively poor prognosis, although the prognosis was largely independent of microsatellite status. This means that the MSI/TIL-L and MSS/TIL-L subtypes had a similarly poor treatment outcome.

"The meta-analysis suggests that combined MSI/TIL testing could be superior to isolated testing for MSI in routine diagnostics," says Hoffmeister.

Wankhede adds, "At the same time, long-term studies should be initiated to evaluate the significance of this marker combination with regard to the chances of success of adjuvant chemotherapy in early colorectal cancer stages."

A commentary on the meta-analysis in the journal *The Lancet Gastroenterology & Hepatology* states, "The integration of MSI-TIL assessment could represent a step forward in personalized treatment strategies."

More information: Durgesh Wankhede et al, Clinical significance of combined tumour-infiltrating lymphocytes and microsatellite instability status in colorectal cancer: a systematic review and network meta-analysis, *The Lancet Gastroenterology & Hepatology* (2024). DOI: 10.1016/S2468-1253(24)00091-8

Provided by German Cancer Research Center

Citation: Combining two tumor markers can help track down colorectal cancer subtypes (2024, May 16) retrieved 17 July 2024 from https://medicalxpress.com/news/2024-05-combining-tumor-markers-track-colorectal.html

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.