New test more effective at predicting survival in blood cancer patients

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Technology that can detect the length of small DNA structures in cancer cells could hold the key to predicting the outcome of patients with two different types of blood cancer. The test, used in conjunction with current methods, may help doctors make better choices about the most appropriate and effective treatment option for individual patients.

Researchers from Cardiff University's School of Medicine showed that measuring sections of DNA called telomeres is a highly accurate indicator of how disease will progress in patients with the bone marrow cancer myeloma and pre-leukaemia myelodysplastic syndromes (MDS) – a bone marrow disorder often leading to life threatening bone marrow failure and even acute myeloid leukaemia (AML).

Results from two studies, which were funded by the charities Bloodwise and Cancer Research UK, are published in new papers in the *British Journal of Haematology*.

The Cardiff team analysed samples from 134 myeloma patients, 80 MDS patients and 95 AML patients to see whether telomere length influences survival in these blood cancers.

Telomeres are protective stretches of DNA that cap the end of chromosomes, and act like plastic tips on shoelaces preventing chromosome ends from fraying and sticking to each other. Every time a cell divides the telomeres gradually shorten and eventually leave the chromosome ends exposed, triggering large-scale DNA damage that

accelerates cancer progression and drug resistance.

After extracting chromosomes from the patients' cancer cells, the researchers measured telomere length in each sample using a technology they had previously developed called Single Telomere Length Analysis (STELA). Telomere length was then checked against patients' medical records to analyse its impact on disease progression and survival.

Currently, patients with myeloma are assessed at diagnosis as 'good', 'standard' and 'high' risk, based on age, overall health and levels of specific proteins in the blood and certain chromosomal abnormalities. The risk categories are used to provide guidance on the intensity of treatment needed for each patient and also indicate survival times. Patients with MDS have a similar assessment, based on chromosomal changes and through an analysis of blood cells in the bone marrow.

The researchers found that while the current system was generally a good indicator of survival times, telomere length had a significant independent impact on survival.

Myeloma patients who had a 'good' or 'standard' risk score under the current system, but had short telomeres, had the same average survival times as patients in the 'high risk' group who had long, functional telomeres. A total of 55 percent of patients who had long telomeres in the 'good' or 'standard' risk groups lived for over 16 years, compared to just 21 percent of patients in these risk groups who had short telomeres.

Most of the patients with MDS in this study were judged to be 'low risk' under standard assessment, and had only received treatment to control their symptoms. In common with patients with myeloma, the researchers found that differing rates of telomere erosion had a clear impact on survival. Only 7 percent of MDS patients with short telomeres survived for more than eight years compared with 46 percent of patients with long

telomeres.

Professor Duncan Baird, who led the research at Cardiff University's School of Medicine with Professors Chris Fegan and Chris Pepper, said: "We really need to improve the way we predict how an individual patient's myeloma or MDS will behave, as these conditions can vary widely in outcome. Our research provides strong evidence that shortening of telomeres plays a vital role in the progression of these blood cancers and that a significant number of patients should be receiving different levels of treatment. The next step is to assess telomere length in larger studies to establish how it can be integrated into existing assessments that predict patient outcome."

The researchers found that while patients with AML had significantly shorter telomeres than patients with MDS, whether telomeres where shorter or longer than the functioning threshold did not appear to lead to any significant differences in survival times.

More information: Thet Thet Lin et al. Telomere dysfunction accurately predicts clinical outcome in chronic lymphocytic leukaemia, even in patients with early stage disease, *British Journal of Haematology* (2014). DOI: 10.1111/bjh.13023

Provided by Bloodwise