Detecting Lynch syndrome in patients with colorectal cancer

Screening all patients with colorectal cancer is the best strategy for identification of carriers of Lynch syndrome, the most common form of hereditary colorectal cancer. Germline mutations in DNA mismatch repair genes cause this disorder, and diagnostic germline genetic testing is considered for patients with colorectal tumours that have deficiency in mismatch repair.

A recent study of 10 206 patients compared the sensitivity and efficiency of several selection strategies for identification of patients at risk of Lynch syndrome. The most sensitive identification strategy proved to be universal screening of all patients with colorectal cancer by tumour mismatch repair testing.

Improved identification of Lynch syndrome has far-reaching benefits. James Ford (Stanford University, Stanford, CA, USA) said, "a patient diagnosed with Lynch syndrome has an 80% lifetime risk of getting colorectal cancer; for women, there's a 50% lifetime risk of endometrial cancer". He added, "if diagnosed with Lynch syndrome, we can identify other family members who are at risk and start screening them earlier, which improves survival".

According to study author Noralane Lindor (Mayo Clinic in Arizona, Scottsdale, AZ, USA), "there has been controversy about how to most effectively screen colon cancer patients for Lynch syndrome, and figuring out the best strategies has been hindered by lack of good data from large studies on how many cases would be undiagnosed if universal screening of all colon cancer patients is not undertaken. This study merged information on over 10 000 unrelated colon cancer cases from around the world."

She continued, "several alternative laboratory screening strategies were tested against this universal screening approach, and the study provides extremely useful information on the number of cases that would be missed by the other strategies". Such information is important to determine how best to identify patients with Lynch syndrome. "The other strategies would clearly save some time and financial resources and would generate fewer people going through genetic testing who turn out not to have Lynch syndrome. Anything less than screening all patients with colorectal cancer for Lynch syndrome will miss some cases, and this needs to be recognised."

James Ford added, "I am hopeful that this [study] will move more clinical centres toward doing universal testing to identify patients with Lynch syndrome".

Judith A Gilbert

David Mack/Science Photo Library

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For the **screening study** see *JAMA* 2012; **308:** 1555–65

Peripheral-blood stem cells or bone marrow for leukaemia?

A recent phase 3 multicentre randomised clinical trial has shown that although outcome for patients with leukaemia or other haematological malignancies varies according to graft source for transplants from unrelated donors, survival advantage is independent of graft source.

The investigators, from the Blood and Marrow Transplant Clinical Trials Network, compared patients receiving peripheral-blood stem cells (PBSCs; 273 patients) with those given bone marrow (278 patients). All patients were paired with tissue-matched unrelated donors. The analyses revealed no significant differences between groups with respect to overall survival, disease-free survival at 2 years, rate of relapse, mortality unrelated to relapse, and rate of acute graft-versus-host disease (GVHD).

However, extensive chronic GVHD was reported in a significantly higher proportion of patients given PBSCs (48% *vs* 32%; p<0·001). Although 57% of patients given PBSC transplant needed immunosuppressive treatment, only 37% of those in the bone marrow group did. Causes of death in the PBSC group were linked to chronic GVHD. Elihu Estey (University of Washington and Fred Hutchinson Cancer Research Center, Seattle, USA) cautioned against the frequently favoured PBSC approach: "this study suggests that the trend to use peripheral blood rather than bone marrow as the source of cells for unrelated donor transplant is, with some exceptions, not supported by the data". Nevertheless, the study showed a higher total incidence of graft failure in the bone marrow transplant group (9% *vs* 3%), which was the main cause of death in the bone marrow group.

"This was a landmark study that will be very difficult to repeat", commented Daniel Weisdorf, director of the Adult Blood and Marrow Transplant Program, University of Minnesota. He added, "we learned about conditional reasons to think that different graft sources might be better for some patients, but also learned that both provide encouraging outcomes for the transplant recipients". The authors suggest that PBSCs should be recommended for patients at high risk of graft failure (those who had never undergone chemotherapy), while bone marrow should be used for all other patients (notably immunosuppressed chemotherapy patients, since they have a lower risk of graft rejection).

Ramla Benmaamar

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