with a primary tumour of 1 cm or less, systemic therapy reduces the rate of distant metastases from 10% to 7%. Although this is a risk reduction of 40%, it means, in effect, that an average of only 3 women on average in every 100 actually benefit from the therapy.[1] Thus, many women may needlessly undergo chemotherapy. However, if distant metastatic disease could be detected at the time of initial cancer diagnosis, the precision of prognostic stratification might be improved. A new technique to detect bone marrow micrometastatic lesions is now available.

Question

What proportion of women presenting with stage I, II or III breast cancer have distant metastatic disease?

Design

Bone marrow aspirates from the upper iliac crests were obtained from 743 consecutive patients admitted to a breast clinic in Germany; 552 had been newly diagnosed with stage I, II or III breast cancer and 191 patients with nonmalignant disease (mainly of the breast). The patients were followed for several years, thus providing some information on the test's usefulness in categorizing women into meaningful risk groups.

Results

Using an immunocytochemical technique to detect an antigen on cytokeratin peptides (a specific marker of epithelial cancer cells in bone marrow), 36% of the women with breast cancer tested positive, compared with only 1% of women without breast cancer. During a median follow-up period of 38 months, women with marrow-detectable cytokeratins were much more likely to die of cancer-related causes than women without the markers (relative risk 4.17; 95% confidence interval 2.51–6.94; $p < 0.001$). There were 301 women with no detectable lymph-node metastastes. Cytokeratin markers were found in the bone marrow of 23% of women with tumours smaller than 0.5 cm and 35% of those with tumours 0.5 to 1.0 cm. Of the 100 patients with node-negative tumours and evidence of micrometastases, 14 died of cancer-related causes over the follow-up period, compared with only 2 of the 201 women without micrometastases.

Commentary

This is a carefully conducted study of a large cohort of women. The testing for cytokeratins was done independently from the clinical staging. However, follow-up was relatively short, especially for a disease such as breast cancer.

Clinical implications

In a related editorial,[1] Barbara Smith comments that it is now important to proceed with trials of therapy because the follow-up is relatively short for breast cancer. Nonetheless, the survival curves extending to 48 months show a continuous divergence of survival and disease-free survival between groups with and without micrometastases. Smith feels that it is premature to recommend cytokeratin tests to patients with disease limited to the breast who wish to avoid chemotherapy. — *John Hoey*, CMAJ

Reference

1. Smith BL. Approaches to breast-cancer screening. *N Engl J Med* 2000;342(8):580-1.

Amok enzymes damage tissues during heart attack

A team of University of Alberta researchers has discovered a cause of the tissue damage that occurs during heart attacks and, in the process, added a wrinkle to current thought on the role of bacterial infections in heart disease (*Circulation* 2000;101:1833).

Led by Dr. Richard Schulz, an Alberta Heritage researcher, the team has come up with striking evidence that the enzyme matrix metalloproteinase-2 (MMP) is responsible for some injuries to heart tissues in the seconds following the onset of a heart attack. What's more, the authors say a novel side effect of tetracycline-class antibiotics that inhibits the action of MMPs must be taken into consideration by researchers probing the involvement of bacteria in heart attacks.

Schulz likens the role of MMPs to a bulldozer parked in your garage — the garage being one of your cardiac muscle cells. In an experimental model of heart attack in rat hearts, the researchers discovered that MMPs, commonly associated with wound healing, were responsible for injury. Beginning mere seconds after the onset of a heart attack, MMPs run amok. It is, Schulz says, as if someone was driving the bulldozer around inside the garage, causing tremendous damage.

They discovered that tetracycline-class antibiotics block the action of MMPs during heart attacks and reduce damage. The drugs can be modified to inhibit only MMPs, so that their use for nonbacterial conditions such as this would not add to the problem of bacterial resistance to antibiotic drugs.

"The question now is for those people who are susceptible to heart attacks — for example, patients with a previous history or angina — whether this class of inhibitors could be used as a prophylactic measure." Other research has drawn links between bacteria and heart attacks. Schulz's team hasn't disproved any connection, but he says its findings cannot be ignored.

"The bacteria angle needs a lot more research," he says. "It really captures the imagination of researchers. People are saying 'Maybe we will find a bacteria that causes some forms of heart attack,' and they may be right. But we are just saying there are novel protective elements of tetracyclines that you have to consider." — *Richard Cairney*, Devon, Alta.