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High white blood cell ratio linked to recurrence risk in early stage breast cancer

*This might guide treatment and monitoring strategies, if prospective studies confirm link*

A high ratio of two types of immune system cell is linked to an increased risk of disease recurrence after a diagnosis of early stage breast cancer, finds the first study of its kind, published on the eve of international Women's Day (March 8) in the online journal *ESMO Open*.

The finding might guide future treatment and monitoring strategies, if prospective studies confirm the link, say the researchers.

A mounting body of evidence indicates that inflammation has a role in the development and progression of several types of cancer, with studies suggesting that the ratio of neutrophils to lymphocytes, or NLR for short, may be important.

Neutrophils and lymphocytes are white blood cells that are despatched as part of the body's immune system response to harmful invaders, including cancer cells.

Several studies have reported that a high NLR is associated with a poor outcome in several different types of cancer. But the few studies carried out in women with breast cancer have been inconclusive--possibly because they have included mostly women of Asian ethnicity whose survival is generally longer than that of women from other ethnic backgrounds, say the researchers.

To find out if NLR was associated with disease free survival, the research team tracked the health of 300 white women, all but nine of whom were older than 35, for up to 15 years (1999-2015) following their diagnosis.

All the women had early stage breast cancer, defined as stages I or II, with no spread to other parts of the body.

On the basis of their blood counts taken after diagnosis, but before treatment, 134 of the women had a low NLR (1.97 or lower) and 166 had a high NLR (above 1.97).

After 15 years, cancer had returned in another part of the body in 37 (12%) of the women.

Women with a low NLR fared better at each of the subsequent check-ups at 1, 3, 6, 9, 12, and 15 years, with, respectively, 100%, 98.9%, 91.7%, 82.7%, 82.7%, and 82.7% of them free of recurrence.

This compares with comparable figures of 99.4%, 94.3%, 84.5%, 69.2%, 66%, and 51.4% at the same time points in those with a high NLR.

The researchers undertook further analysis to take account of other potentially influential factors. They found that not having yet gone through menopause, nodes with cancerous cells in the armpit (N1), and a high NLR were independently associated with the risk of recurrence.

To corroborate the findings further, the researchers carried out a propensity score matched analysis--a statistical matching technique that attempts to estimate the effect of an intervention by accounting for the factors that predict receiving it.

This technique was applied to 226 patients (half with a high NLR and half with a low NLR).The results confirmed that not having gone through the menopause, having armpit lymph nodes with cancerous cells, and a high NLR were each independently associated with a worse prognosis.

This is an observational study so no firm conclusions can be drawn about cause and effect, and it was retrospective. But the statistical matching strengthens the associations found, which have also been found in other cancers, say the researchers.

"Despite looking apparently simple, the relationship between NLR and outcome in patients with cancer is probably a complex and multifactorial process [that is] still poorly understood," write the researchers.

"In simple terms, a high NLR may reflect the key role of systemic inflammation in enhancing angiogenesis [formation of new blood vessels], tumour growth, and development of metastasis [spread]," they say.

*ESMO Open* Editor in Chief, Professor Christoph Zielinski, comments: "It is inspirational to see the results of this study showing that there may be a potential new way to support women with early breast cancer. We hope that it will encourage more researchers active in this area to establish collaborations around the world with a view to confirming these findings."

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