The mode of detection of high-risk breast cancers is linked to patient prognosis

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Breast cancers that are detected in the interval between national screening programme mammograms have a worse prognosis than those detected at the time of a screening, even if they have the same biology, according to research presented at the 12th European Breast Cancer Conference on Saturday.

Analysis of results from over eight years' follow-up of the international MINDACT randomised phase III clinical trial shows that although tumours may have the same genetic make-up, the way they are detected makes a significant difference to the period of time before the disease starts spreading to other parts of the body or results in death, whichever comes first. This is known as the distant metastasis-free interval (DMFI).

Dr. Josephine Lopes Cardozo (MD), a Ph.D. candidate at the Netherlands Cancer Institute (NKI) in Amsterdam, The Netherlands, and medical fellow at the European Organisation for Research and Treatment of Cancer (EORTC) in Brussels, Belgium, told the conference that the method of detection gave additional prognostic information and should be taken into account when deciding on what treatments in addition to surgery might be needed.

Dr. Lopes Cardozo and her colleagues had found previously that tumours that occurred in the interval between screening mammographies, known as interval cancers, were more likely to have a high-risk genetic profile, as shown by a test that looks at the activity of 70 genes in the tumour tissue (the 70-gene signature, commercially known as MammaPrint), and

were therefore at higher risk of distant metastases.

"However, there are also screen-detected cancers with a high-risk 70-gene signature," she said. "In our current analysis, we found a significant difference in survival between high-risk cancers detected during screening or in the interval between screenings. The eight-year DMFI rate was higher among women with screen-detected cancers than for women with interval cancers: 93.8% versus 85.2%.

"Although these tumours have the same biology—all 70-gene, high-risk and with similar tumour characteristics—they have different prognoses based on their method of detection. This suggests that the method of detection is an additional prognostic factor in this group of patients. The method of detection combined with the 70-gene signature can further optimise treatment for patients at high risk of recurrence. For patients with a very low risk of recurrence, longer follow-up may also help to identify those who are currently at risk of being over-treated."

A total of 1102 Dutch breast cancer patients enrolled in the MINDACT trial between 2007 and 2011, who participated in the national screening programme and who were aged 50-75, were included in the analysis. The Dutch national screening programme invites women aged 50-75 years for screening every two years. The researchers evaluated differences in DMFI for high, low and ultra-low risk tumours, as classified by the 70-gene signature. A total of 754 cases were detected during screening, and 348 during the interval between screenings.

With 50% of patients having reached at least 8.6 years of follow-up, there were 83 occurrences of distant metastases or death due to breast cancer. Among patients with screen-detected cancers, 36% received no adjuvant systemic treatment (such as chemotherapy and hormone therapy, in addition to surgery and radiotherapy), 33% received hormone therapy only and 30% received chemotherapy with or without hormone

therapy. Among patients with interval cancers, 17% received no adjuvant systemic treatment, 35% had hormone therapy only and 47% had chemotherapy with or without hormone therapy.

"Most patients who received no adjuvant systemic therapy had grade I tumours, smaller than 2cms, had no signs of cancer in their lymph nodes and were classified as ultra-low or low risk by the 70-gene signature," said Dr. Lopes Cardozo.

When the researchers looked at survival rates at eight years, they found that patients with screen-detected cancers had an eight-year DMFI rate of 98.2% in 118 women with ultra-low-risk tumours, 94.6% in the 398 women with low-risk tumours, and 93.8% in the 238 women with high-risk tumours.

Patients with interval cancers had an eight-year DMFI rate of 97.4% in the 39 women with ultra-low-risk tumours, 92.2% in the 143 women with low-risk tumours, and 85.2% in the 166 women with high-risk tumours.

Among patients with high-risk tumours, those that were detected in the interval between screenings had a 2.4-fold increased chance of developing distant metastases compared to those whose cancer was detected during screening.

Dr. Lopes Cardozo concluded: "Both screen-detected and interval breast cancers have very good eight-year distant metastasis-free interval rates. However, among patients with high-risk tumours as classified by the 70-gene signature, there is a significant difference in these rates between screen-detected and interval cancers. Combining the prognostic information provided by the 70-gene signature and the method of detection can help to choose the best treatment for these patients."

Professor David Cameron, from the University of Edinburgh Cancer Centre, UK, who represents the European Breast Cancer Council at EBCC12, was not involved with the research. He commented: "This study highlights an interesting difference between breast cancers that are detected at the time a woman attends a scheduled appointment as part of a national screening programme (screen detected) and those that are diagnosed in the interval between screenings (interval cancers). It has been previously noted that interval cancers are more likely to be high grade and that would be associated with a poorer outcome, but the novel finding here is that for those cancers identified biologically as being high risk by the 70-gene signature test, the screen detected ones do better than those presenting as interval cancers.

"If these results are confirmed in another series, it would suggest that earlier diagnosis via screening of more biologically aggressive cancers is worthwhile: screen-detecting such cancers may improve patients' survival. The findings also suggest that clinicians should take into account the method of detection as an additional prognostic factor when considering adjuvant therapy, enabling further personalisation of therapy to the individual woman and her cancer. This is as important for low-risk cancers as for high-risk ones. Longer follow-up for low-risk cancers could give us more information as to whether more aggressive treatments could be avoided, as these tumours can recur 15 to 20 years later."

More information: Abstract no: 11, "Screen-detected breast cancers have different tumour biology and better prognosis compared to interval breast cancers", Proffered papers session, Saturday 13.15-15.00 hrs, Channel 3 (Dr Lopes Cardozo's presentation will be at 13.45 hrs).

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