Psychosocial factors and the incidence of breast cancer: two-stage individual participant data meta-analyses

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POSTER DISCUSSION SESSION 17 November 2022 16.00–16.50

Poster Discussion Session 2

9 (PB-005) Poster Discussion

Forty-eight weeks of yogic intervention improves serum interleukins IL-10 and IL-1β along with fatigue and quality of life during the radiotherapy/chemotherapy in breast cancer patients: a randomized control study

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Background: Yoga improved fatigue and immunological profile in cancer survivors and has been a promising alternative therapy. Breast cancer treatments are rapidly improving along with their side effects. In this study we investigated the effect of the yogic intervention at a different time interval during the radiotherapy/chemotherapy on the pro and anti-inflammatory interleukins along with the fatigue and quality of life among patients with stage II/III breast cancer.

Methods: A total of 96 stage II/III breast cancer patients were enrolled in this study and randomly divided into two different groups. Group-I (non-Yoga) received chemotherapy and/or radiotherapy and group II (Yoga) received an additional yogic intervention. Both the groups were followed up for a period of 48 weeks and blood was collected at the time of enrollment, 16, 32, and 48 weeks and serum were isolated to measure the pro and anti inflammatory interleukins, fatigue, and functional scale questionnaire was obtained at each time point. We have also used the validated questionnaire of the European Organization for Research and Treatment of Cancer to measure the quality of life (EORTC-QLQ30) of breast cancer patients.

Result: In group II functional scale was improved from the baseline to 16, 32, and 48 weeks were 44.49 ± 2.31, 55.64 ± 2.09, 60.8 ± 1.96, 72.14 ± 1.79 respectively. Whereas in group-I overall little improvement was also recorded from baseline 46.27 ± 1.76 to 48 weeks 54.43 ± 2.38. In group-II fatigue was also improved from the baseline to 16, 32, and 48 weeks were 42.38 ± 2.70, 54.9 ± 2.79, 58.33 ± 2.61, 62.44 ± 2.58 respectively and overall little improvement was also recorded in the group-I from baseline 42.18 ± 2.81 to 48 weeks 50.95 ± 3.20. In group-II overall quality of life was improved from the baseline to 16, 32, and 48 weeks were 37.33 ± 1.33, 39.87 ± 2.99, 38.79 ± 3.23, 74 ± 1.59 respectively. Whereas the poor quality of life was recorded in the group-I during treatment from baseline (39.51 ± 0.96) to 48 weeks (20.51 ± 1.57). Level of IL-1β (pg/ml) decreased significantly from 69.77 ± 2.62 to 61.16 ± 3.41 (p = 0.001) in group-II (baseline to 48 weeks) whereas an increase in the group-I (baseline to 48 weeks) was recorded from 73.14 ± 2.66 to 81.13 ± 2.04 (p = 0.35). The level of IL-10 (pg/ml) decreased significantly from 10.47 ± 1.10 to 4.855 ± 0.81 (p = 0.001) in group-II (baseline to 48 weeks) whereas a slight decrease was recorded in the group-I (baseline to 48 weeks) was recorded from 10.97 ± 0.83 to 9.385 ± 1.216 (p = 0.35).

Conclusion: These finding suggested that improved fatigue and functional scale is associated with a lower level of IL-1β. Yoga may be important additional therapy along with the cancer treatment to help the patients with cancer-related fatigue and improve their overall immunological profile and overall quality of life during treatment.

No conflict of interest.

10 (PB-006) Poster Discussion

Long-term breast cancer risk after benign breast disease in population-based screening

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Background: To assess the long-term risk of breast cancer after benign breast disease diagnosed through breast screening.

Methods: We analysed individual-level data from 778 306 women aged 50–69 years with at least one mammographic screening participation in ten Breast Cancer Screening centres in Spain from 1996 to 2015 and followed-up until 2017. We compared rates of incident breast cancer among women with and without benign breast disease. We calculated crude and adjusted rate ratios to compare both groups. Poisson regression was used for adjusted analyses.

Results: By December 2017, 242 557 women had been followed for up to 4 years, 179 167 for 5–8 years, 188 399 for 9–12 years, 150 356 for more than 12 years. Over the study period, 17 827 women were diagnosed with benign breast disease and 11 708 women had an incident breast cancer, corresponding to an incidence rate of 14.8 (95% CI 14.5 to 15.1) per 1000 women among those without a benign breast disease; and 24.8 (95% CI 22.6 to 27.2) among those with a benign breast disease. Women with benign breast disease had an overall increased relative risk of 1.77 (95%CI: 1.61 to 1.95). The excess risk in women with benign breast disease remained increased over time, with relative risk 1.99 (95%CI: 1.73 to 2.29) for those followed less than 4 years, to 1.96 (95%CI: 1.32 to 2.92) for those followed 12 to 20 years. The excess incidence risk was independent of year at mammography or age at mammography.

Table: Crude and adjusted rate ratios of incidence breast cancer in women with benign breast disease at screening, according to year, age, and time since index mammogram.

	No Benign Breast Disease Cases/ Women	Benign Breast Disease Cases/ Women	Crude Ratio (95%CI)	Adjusted Ratio (95%CI)
Year at index mammogram				
1996–2000	2 776/117 837	95/2 287	1.76 (1.44–2.16)	1.49 (1.21–1.82)
2001–2005	5 042/237 613	156/3 985	1.84 (1.57–2.16)	1.57 (1.34–1.85)
2006–2010	2 715/210 947	128/5 156	1.93 (1.62–2.30)	1.95 (1.64–2.33)
2011–2015	733/194 082	63/6 399	2.61 (2.02–3.37)	3.11 (2.41–4.03)
Age at index mammogram				
50–54	6 477/455 833	233/8 926	1.84 (1.61–2.09)	1.68 (1.47–1.91)
55–59	2 938/146 256	107/3 773	1.41 (1.16–1.71)	1.53 (1.26–1.86)
60–64	1 645/118 008	79/3 152	1.80 (1.43–2.25)	2.38 (1.90–2.98)
65–69	206/40 382	23/1 976	2.28 (1.48–3.51)	3.25 (2.11–5.00)
Time since index mammogram				
≤4 years	4 096/242 557	201/7 582	1.57 (1.36–1.81)	1.99 (1.73–2.29)
>4 and ≤8 years	3 990/179 167	147/4 662	1.42 (1.20–1.67)	1.58 (1.34–1.86)
>8 and ≤12 years	2 337/188 399	69/3 361	1.66 (1.30–2.10)	1.64 (1.29–2.08)
>12 years	843/150 356	25/2 222	2.01 (1.35–2.99)	1.96 (1.32–2.92)

Conclusion: Women with benign breast disease experienced higher long-term risks of breast cancer than women with negative screens for two decades. Women with benign breast disease could benefit from closer surveillance and more personalised screening strategies.

No conflict of interest.

11 (PB-007) Poster Discussion

Psychosocial factors and the incidence of breast cancer: two-stage individual participant data meta-analyses

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Netherlands; [7]University Medical Center Groningen, Department of Psychiatry, Groningen, Netherlands

Background: Over the last decades, it has been repeatedly suggested that psychosocial factors such as depression and anxiety increase the risk of breast cancer, through mechanisms such as mutation, DNA repair, neuroendocrine processes, immunological processes, or unhealthy behaviours. With individual participant data meta-analyses, we aimed to test whether depression, anxiety, recent loss event, and perceived social support increase the risk for breast cancer. We also explored the effects of neuroticism, general distress, and relationship status.

Materials and methods: IPD meta-analyses were performed with up to twenty-two studies in the PSY-CA consortium (up to: N = 220,258, person years = 2,502,822, breast cancer incidences = 5724). At stage 1, Cox regression models were fitted in each cohort for each psychosocial factor (outlined above) and breast cancer outcome. Two models were tested: a minimally-adjusted model (correcting for sociodemographic covariates) and a maximally-adjusted model (additionally correcting for several health behaviors and other potential confounders such as parity). At stage 2, hazard ratios (from stage 1) were pooled using random-effects meta-analyses.

Results: Most psychosocial factors were not related to breast cancer incidence, with the exception of anxiety symptoms which showed a protective effect (HR = 0.95 [0.91, 0.998], $p = 0.04$) in the minimally adjusted model. When adjusting for further potential confounders, this effect was no longer statistically significant (HR = 0.96 [0.90, 1.02], $p = 0.14$).

Conclusions: We found no consistent evidence for an association between psychosocial factors and the incidence of breast cancer, with the possible exception of anxiety symptoms showing a small, protective effect. Further research is needed to test whether health-related behaviours, such as unhealthy behaviours or menopausal status, moderate the association between psychosocial factors and breast cancer.

No conflict of interest.

12 (PB-008) Poster Discussion

Effectiveness of a nurse-navigation intervention in vulnerable breast cancer patients – The Rebecca Study

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Background: Women with breast cancer may suffer from adverse effects of treatment including psychological distress, anxiety, and depression as well as physical symptoms such as pain and fatigue. Despite available rehabilitation services breast cancer patients still report unmet needs for support.

The aim of this study was to evaluate the effectiveness of the REBECCA intervention combining nurse navigation and systematic screening for psychological and physical symptoms in vulnerable breast cancer patients using a randomized controlled design.

Material and Methods: Between 2017–2019 all eligible patients were invited consecutively to participate in the study by a project nurse. Enrolled patients reporting moderate to severe distress at baseline were randomized using a computer-generated assignment 1:1 to either standard care or to the REBECCA intervention. The intervention comprised repeated screening using patient reported outcome measures and up to 8 individual nurse navigation sessions providing psychoeducation, support, and referrals to symptom management.

Questionnaire data was collected at baseline before surgery and, 6, 12 and 18 months after. Primary outcome was distress. Secondary outcomes were e.g., anxiety, depression, and breast cancer specific health related quality of life (HQoL). In intention to treat analyses (ITT), we applied linear mixed regression models with 95% confidence intervals to examine the effect of the intervention on primary outcomes at the four time points. Effect sizes were evaluated using Cohens d.

Results: We identified 309 vulnerable patients with breast cancer who were randomly assigned to the intervention (N = 153) or the control (N = 156). Overall intervention effects were seen for depression ($p = 0.037$) and breast cancer specific HQoL ($p = 0.03$) and a borderline significant intervention effect was seen for anxiety ($p = 0.062$) with strongest effects at either 6 or 12 months follow-up.

Larger effects were seen in adjusted analyses. Patients receiving the REBECCA intervention, compared to standard care had significantly reduced symptoms of distress at 12 months follow-up in the adjusted analyses. Furthermore, significant effects were seen in adjusted analyses for symptoms of anxiety at 6, 12 and 18 months, depression at 6 months, HQoL at 6 and 12 months and for fear of recurrence at 6 and 12 months. The effects were modified by age, patient activation, education, and social support.

Conclusions: The REBECCA intervention did have positive effects on several psychological and physical outcomes. The REBECCA intervention improved symptoms of depression, breast cancer related quality of life and to some extent anxiety. Socially vulnerable sub-groups may have the largest benefit.

Our findings merit further research to refine the nurse navigation framework further.

No conflict of interest.

13 (PB-009) Poster Discussion

External validation and clinical utility assessment of PREDICT v2.2 prognostic model in young, node-negative, systemic treatment-naïve breast cancer patients

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Background: The PREDICT breast prognostic model is widely used by oncologists for decision-making about systemic treatment for breast cancer patients. However, whether PREDICT could provide accurate predictions before systemic treatment in young patients remains unclear. This study assessed the validity and clinical utility of the latest version of PREDICT (v2.2) in young, node-negative, breast cancer patients who did not receive systemic treatment.

Methods: We selected all women from the Netherlands Cancer Registry, diagnosed with node-negative breast cancer under 40 years of age between 1989 and 2000; a period when national guidelines did not recommend the use of systemic treatment for node-negative patients. The validity of PREDICT to predict all-cause mortality was assessed through calibration and discrimination, calculated as the ratio of observed and expected all-cause mortality (O/E ratio), and the area under the receiver-operating-characteristic-curve (AUC) at 10 years, respectively. Clinical utility of PREDICT was evaluated using decision curve analysis and compared to the clinical utility of the European Society of Medical Oncology (ESMO) guideline. Predefined thresholds for estrogen receptor (ER)-positive and ER-negative patients were based on the MINDACT trial, where adjuvant chemotherapy was recommended to patients with a predicted 10-year all-cause mortality $\geq$8% (ER-negative) or $\geq$12% (ER-positive). Clinical utility was represented by net benefit, calculated as the rate of correctly predicted high-risk patients who should receive chemotherapy minus the weighted (odds of the threshold) rate of falsely predicted high-risk patients who should not receive chemotherapy.

Results: We included 2,264 patients with a median age at diagnosis of 36 years. Most patients had ER-positive (70.9%), and grade 1–2 tumors (56.2%); the median tumor size was 16 mm. Observed 10-year all-cause mortality for all patients was 32% higher than the predicted value (table), which was likely due to earlier years of diagnosis of the study population compared to the PREDICT derivation cohort. PREDICT had a 65% chance (AUC) to correctly separate patients who would and would not die within 10 years. Compared to the ESMO guideline, PREDICT only showed slightly higher net benefit in ER-positive patients.