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BREAST CANCER RESEARCH AND TREATMENT

1.-
Effects of physical exercise after treatment of early breast cancer: systematic review and meta-analysis.
Soares Falcetta, F.; de Araújo Vianna Träsel, H.; de Almeida, F.K.; Rangel Ribeiro Falcetta, M.; Falavigna, M.; Dornelles Rosa, D.
Vol. 170 Nr. 3 Página: 455 - 476 Fecha de publicación: 01/08/2018
Resumen:
PURPOSE: Randomized clinical trials are inconclusive regarding the role of physical exercise in anthropometric measurements, quality of life, and survival in breast cancer patients. Our aim was to conduct a systematic review and meta-analysis to assess the effects of physical exercise on these outcomes in women who went through curative treatment of early-stage breast cancer. METHODS: Pubmed, Embase, Cochrane Library were searched for randomized clinical trial comparing physical exercise (counseling or structured programs with supervised/individualized exercise sessions) with usual care in women that went through for breast cancer treatment. Primary outcomes were overall survival and disease-free survival, while secondary outcomes were weight loss, body mass index, waist-hip ratio, percentage of body fat, and quality of life. RESULTS: We found 60 randomized clinical trials, only one of them showed mortality data; the HR for mortality was 0.45 (95% CI 0.21-0.97) for the intervention group when compared to the control group. Physical exercise was associated with weight reduction (- 1.36 kg, 95% CI - 2.51 to - 0.21, p = 0.02), lower body mass index (- 0.89 kg/m², 95% CI - 1.50 to - 0.28, p < 0.01), and lower percentage of body fat (- 1.60 percentage points, 95% CI - 2.31 to - 0.88, p < 0.01). There was an increase in the quality of life (standardized mean difference of 0.45, 95% CI 0.20-0.69, p < 0.01). CONCLUSIONS: The articles found had heterogeneous types of intervention, but they showed significant effects on anthropometric measures and quality of life. Among them, only one study had mortality as outcome and it showed physical exercise as a protective intervention. Despite these findings, publication bias and poor methodological quality were presented. Physical exercise should be advised for breast cancer survivors since it has no adverse effects and can improve anthropometrics measures and quality of life. PROSPERO registry: CRD42014008743.

2.-
MCP-1 is overexpressed in triple-negative breast cancers and drives cancer invasiveness and metastasis.
Dutta, P.; Sarkissyan, M.; Paico, K.; Wu, Y.; Vadgama, J.V.
Vol. 170 Nr. 3 Página: 477 - 486 Fecha de publicación: 01/08/2018
Resumen:
BACKGROUND: Triple-negative breast cancer (TNBC) is the most aggressive type of breast cancer that lacks ER/PR and HER2 receptors. Hence, there is urgency in developing new or novel therapeutic strategies for treatment of TNBC. Our study shows that the Monocyte Chemoattractant Protein-1 (MCP-1) is a marker associated with TNBC and may play a key role in TNBC disease progression. EXPERIMENTAL DESIGN: ELISA method was used to measure secreted MCP-1, and mRNA levels were determined by Real-time PCR in numerous cancer cell lines, representing various breast cancer subtypes. Cellular invasiveness was determined by Boyden chamber assay. RESULTS: Our data show that MCP-1 is upregulated in TNBC cell lines both transcriptionally as well as in secreted protein levels compared to ER-positive luminal cell line, MCF-7. Breast cancer patients, with Basal or Claudin-low subtypes, also showed high expression of MCP-1. MCP-1 treatment induced cell invasion in various breast cancer cell types, without affecting cell proliferation. Small molecule antagonists against Chemokine Receptor 2 (CCR2), cognate receptor for MCP-1 as well as the MAP kinase pathway inhibitor U0126 negatively affected MCP-1 induced MCF-7 cell invasion. This suggests that MCP-1-CCR2 axis may regulate invasiveness via the MAP Kinase pathway. Knocking down MCP-1 decreased cell invasion in TNBC cell line BT-549, along with downregulation of key epithelial to mesenchymal transition markers, N-cadherin and Vimentin. CONCLUSION: Our study suggests that MCP-1 mediated pathways could be potential therapeutic targets for the treatment of TNBC, and could reduce cancer health disparities.

3.-
Association of reproductive history with breast tissue characteristics and receptor status in the normal breast.
Gabrielson, M.; Chiesa, F.; Behmer, C.; Rönnow, K.; Czene, K.; Hall, P.
Vol. 170 Nr. 3 Página: 487 - 497 Fecha de publicación: 01/08/2018
Resumen:
INTRODUCTION: Reproductive history has been associated with breast cancer risk, but more knowledge of the underlying biological mechanisms is needed. Because of limited data on normal breast tissue from healthy women, we examined associations of reproductive history and established breast cancer risk factors with breast tissue composition and markers of hormone receptors and proliferation in a nested study within the Karolinska Mammography project for risk prediction for breast cancer (Karma). MATERIALS AND METHODS: Tissues from 153 women were obtained by ultrasound-guided core needle biopsy as part of the Karma project. Immunohistochemical staining was used to assessed histological composition of epithelial, stromal and adipose tissue, epithelial and stromal oestrogen receptor (ER) and progesterone receptor (PR) status, and Ki-67 proliferation status. An individualised reproductive score including parity, number of pregnancies without birth, number of births, age at first birth, and duration of breastfeeding, was calculated based on self-reported reproductive history at the time of the Karma study entry. All analyses were adjusted for age and BMI. RESULTS: Cumulated reproductive score was associated with increased total epithelial content and greater expression of epithelial ER. Parity was associated with greater epithelial area, increased epithelial-stromal ratio, greater epithelial ER expression and a lower extent of stromal proliferation. Increasing numbers of pregnancies and births were associated with a greater epithelial area in the entire study set, which remained significant among postmenopausal women. Increasing numbers of pregnancies and births were also associated with a greater expression of epithelial ER among postmenopausal women. Longer duration of breastfeeding was associated with greater epithelial area and greater expression of epithelial PR both in the entire study set and among postmenopausal women. Breastfeeding was also positively associated with greater epithelial ER expression among postmenopausal women. Prior use of oral contraceptives was associated with lower epithelial-stromal ratio amongst all participants and among pre- and postmenopausal women separately. CONCLUSION: Reproductive risk factors significantly influence the epithelial tissue compartment and expression of hormone receptors in later life. These changes remain after menopause. This study provides deeper insights of the biological mechanisms by which reproductive history influences epithelial area and expression of hormone receptors, and as a consequence the risk of breast cancer.

4.-
Randomized trial of proactive rapid genetic counseling versus usual care for newly diagnosed breast cancer patients.
Schwartz, M.D.; Peshkin, B.N.; Isaacs, C.; Willey, S.; Valdimarsdottir, H.B.; Nusbaum, R.; Hooker, G.; O'Neill, S.; Jandorf, L.; Kelly, S.P.; Heinzmann, J.; Zidell, A.; Khoury, K.
Vol. 170 Nr. 3 Página: 517 - 524 Fecha de publicación: 01/08/2018
Resumen:
PURPOSE: Breast cancer patients who carry BRCA1/BRCA2 gene mutations may consider bilateral mastectomy. Having bilateral mastectomy at the time of diagnosis not only reduces risk of a contralateral breast cancer, but can eliminate the need for radiation therapy and yield improved reconstruction options. However, most patients do not receive genetic counseling or testing at the time of their diagnosis. In this trial, we tested proactive rapid genetic counseling and testing (RGCT) in newly diagnosed breast cancer patients in order to facilitate pre-surgical genetic counseling and testing. METHODS: We recruited newly diagnosed breast cancer patients at increased risk for carrying a BRCA1/2 mutation. Of 379 eligible patients who completed a baseline survey, 330 agreed to randomization in a 2:1 ratio to RGCT (n = 220) versus UC (n = 108). Primary outcomes were genetic counseling and testing uptake and breast cancer surgical decisions. RESULTS: RGCT led to higher overall (83.8% vs. 54.6%; p < 0.0001) and pre-surgical (57.8% vs. 38.7%; p = 0.001) genetic counseling uptake compared to UC. Despite higher rates of genetic counseling, RGCT did not differ from UC in overall (54.1% vs. 49.1%, p > 0.10) or pre-surgical (30.6% vs. 27.4%, p > 0.10) receipt of genetic test results nor did they differ in uptake of bilateral mastectomy (26.6% vs. 21.8%, p > 0.10). CONCLUSIONS: Although RGCT yielded increased genetic counseling participation, this did not result in increased rates of pre-surgical genetic testing or impact surgical decisions. These data suggest that those patients most likely to opt for genetic testing at the time of diagnosis are being effectively identified by their surgeons.

5.-
A randomized, double-blind, phase 2 study of ruxolitinib or placebo in combination with capecitabine in patients with advanced HER2-negative breast cancer and elevated C-reactive protein, a marker of systemic inflammation.
O'Shaughnessy, J.; DeMichele, A.; Ma, C.X.; Richards, P.; Yardley, D.A.; Wright, G.S.; Kalinsky, K.; Steis, R.; Diab, S.; Kennealey, G.; Geschwindt, R.; Jiang, W.; Rugo, H.S.
Vol. 170 Nr. 3 Página: 547 - 557 Fecha de publicación: 01/08/2018
Resumen:
PURPOSE: The Janus-associated kinase (JAK)/signal transducer and activator of transcription pathway is a key regulator of inflammatory signaling, associated with tumorigenesis, cell survival, and progression. This randomized phase 2 trial evaluated the efficacy and safety of the addition of ruxolitinib, a JAK1/JAK2 inhibitor, to capecitabine in patients with HER2-negative advanced breast cancer and high systemic inflammation (modified Glasgow Prognostic Score [mGPS] = 1). METHODS: Patients with = 2 prior chemotherapy regimens for advanced or metastatic disease or hormone receptor-positive patients with disease progression on prior hormonal therapies were randomized 1:1 to 21-day cycles of ruxolitinib (n = 76) or placebo (n = 73) plus capecitabine. The primary endpoint was overall survival (OS). RESULTS: Baseline characteristics were well balanced between groups. For ruxolitinib plus capecitabine versus placebo plus capecitabine, median OS was 11.2 months versus 10.9 months (log-rank test P = 0.762); median progression-free survival (PFS) was 4.5 months versus 2.5 months (log-rank test P = 0.151); and overall response rate (ORR) was 28.9% versus 13.7% (Cochran-Mantel-Haenszel test P = 0.024), respectively. A more favorable change in health-related quality of life (HRQoL) was observed with ruxolitinib plus capecitabine versus placebo plus capecitabine. Both regimens were generally tolerable. A higher incidence of grade 3/4 anemia (25.4% vs 5.6%) and a lower incidence of grade 3/4 palmar-plantar erythrodysesthesia (1.4% vs 12.7%) occurred with ruxolitinib plus capecitabine versus placebo plus capecitabine. CONCLUSIONS: The addition of ruxolitinib to capecitabine for patients with advanced breast cancer and high systemic inflammation was generally tolerable; ORR was numerically greater, a more favorable change in HRQoL was observed, but neither OS nor PFS was improved compared with placebo plus capecitabine.

6.-
Response rates and pathologic complete response by breast cancer molecular subtype following neoadjuvant chemotherapy.
Haque, W.; Verma, V.; Hatch, S.; Suzanne Klimberg, V.; Brian Butler, E.; Teh, B.S.
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Resumen:
PURPOSE: This is the largest study to date evaluating response rates and pathologic complete response (pCR) and predictors thereof, based on molecular subtype, in women with breast cancer having undergone neoadjuvant chemotherapy (NC). METHODS: The National Cancer Database was queried for women with cT1-4N1-3M0 breast cancer having received NC. Patients were divided into four subtypes: luminal A, luminal B, Her2, or triple negative (TN). Multivariable logistic regression ascertained factors associated with developing pCR. Kaplan-Meier analysis evaluated overall survival (OS) between patients by degree of response to NC when stratifying patients by subtype. RESULTS: Of a total of 13,939 women, 322 (2%) were luminal A, 5941 (43%) luminal B, 2274 (16%) Her2, and 5402 (39%) TN. Overall, 19% of all patients achieved pCR, the lowest in luminal A (0.3%) and the highest in Her2 (38.7%). Molecular subtype was an independent predictor of both pCR and OS in this population. Clinical downstaging was associated with improved survival, mostly in women with luminal B, Her2, and TN subtypes. Subgroup analysis of the pCR population demonstrated 5-year OS in the luminal B, Her2, and TN cohorts of 93.0, 94.2, and 90.6%, respectively (Her2 vs. TN, p = 0.016). CONCLUSIONS: Assessing nearly 14,000 women from a contemporary United States database, this is the largest known study examining the relationship between response to NC and molecular subtype. Women with luminal A disease are the least likely to undergo pCR, with the highest rates in Her2 disease. Degree of response is associated with OS, especially in luminal B, Her2, and TN patients. Despite the comparatively higher likelihood of achieving pCR in TN cases, this subgroup may still experience a survival detriment, which has implications for an ongoing national randomized trial.

7.-
Impact of port site scar on perception of patients with breast cancer: patient-reported outcomes.
Voci, A.; Lee, D.; Ho, E.; Crane-Okada, R.; DiNome, M.
Vol. 170 Nr. 3 Página: 569 - 572 Fecha de publicación: 01/08/2018
Resumen:
PURPOSE: As the number of survivors continues to increase with improvements in breast cancer treatment, greater emphasis has been placed on the aesthetic outcome following breast surgery. Effort is made to minimize scarring on the breast, yet patients who require a port for treatment inevitably have a scar on the upper chest from the port itself. We hypothesized that patients with breast cancer are conscious of their port scars, and if given a choice would prefer placement of the port in the arm rather than the chest. METHODS: Female breast cancer patients treated at our Breast Center who had a port placed from 2009 to 2015 were asked to complete a 20-question, anonymous survey via SurveyMonkey® reporting demographics and treatment information, and a validated Patient Scar Assessment Questionnaire (PSAQ). RESULTS: Of 139 identified, 105 had email information available for contact, and 67 (64%) patients responded. Of the 67, 37 (55%) had undergone arm placement and 30 (45%), chest. Sixty (92%) patients report noticing their scars; 44 (69%) believed that their scar was noticeable to others; and 22 of the 44 (50%) made an effort to hide their scar. Thirty-seven patients were offered options for port site placement, and 24 (65%) chose placement in the arm (p = 0.057). CONCLUSION: Most patients are conscious of their port scars and if offered the choice choose placement in the arm rather than the chest. Upper extremity port placement should be further explored as an alternative approach for patients with breast cancer to improve port scar consciousness.

8.-
Understanding racial/ethnic differences in breast cancer-related physical well-being: the role of patient-provider interactions.
Check, D.K.; Chawla, N.; Kwan, M.L.; Pinheiro, L.; Roh, J.M.; Ergas, I.J.; Stewart, A.L.; Kolevska, T.; Ambrosone, C.; Kushi, L.H.
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Resumen:
PURPOSE: Racial/ethnic differences in cancer symptom burden are well documented, but limited research has evaluated modifiable factors underlying these differences. Our objective was to examine the role of patient-provider interactions to help explain the relationship between race/ethnicity and cancer-specific physical well-being (PWB) among women with breast cancer. METHODS: The Pathways Study is a prospective cohort study of 4505 women diagnosed with breast cancer at Kaiser Permanente Northern California between 2006 and 2013. Our analysis included white, black, Hispanic, and Asian participants who completed baseline assessments of PWB, measured using the Functional Assessment of Cancer Therapy for Breast Cancer, and patient-provider interactions, measured by the Interpersonal Processes of Care Survey (IPC) (N = 4002). Using stepwise linear regression, we examined associations of race/ethnicity with PWB, and changes in associations when IPC domains were added. RESULTS: We observed racial/ethnic differences in PWB, with minorities reporting lower scores than whites (beta, black: - 1.79; beta, Hispanic: - 1.92; beta, Asian: - 1.68; p < 0.0001 for all comparisons). With the addition of health and demographic covariates to the model, associations between race/ethnicity and PWB score became attenuated for blacks and Asians (beta: - 0.63, p = 0.06; beta: - 0.68, p = 0.02, respectively) and, to a lesser extent, for Hispanic women (beta: - 1.06, p = 0.0003). Adjusting for IPC domains did not affect Hispanic-white differences (beta: - 1.08, p = 0.0002), and slightly attenuated black-white differences (beta: - 0.51, p = 0.14). Asian-white differences narrowed substantially (beta: - 0.31, p = 0.28). CONCLUSIONS: IPC domains, including those capturing perceived discrimination, respect, and clarity of communication, appeared to partly explain PWB differences for black and Asian women. Results highlight opportunities to improve providers' interactions with minority patients, and communication with minority patients about their supportive care needs.

9.-
Pre-diagnostic changes in body mass index and mortality among breast cancer patients.
Larsen, S.B.; Torstensson, M.; Kenborg, L.; Christensen, J.; Kroman, N.; Dalton, S.O.; Tjønneland, A.; Johansen, C.; Bidstrup, P.E.
Vol. 170 Nr. 3 Página: 605 - 612 Fecha de publicación: 01/08/2018
Resumen:
PURPOSE: We investigated whether changes in body mass index (BMI) before a breast cancer diagnosis affected mortality and whether trajectories more accurately predict overall mortality compared to a single measure of BMI. METHODS: Our prospective cohort comprised 2012 women with breast cancer who reported their weight in each decade from 20 to 50-64 years of age. We used trajectory analysis to identify groups with similar development patterns in BMI and Cox proportional hazards models to examine the association between trajectory groups and mortality, and interactions with oestrogen receptor status and smoking. We used c-index statistics to compare the trajectory model with the single measure model of BMI. RESULTS: We identified three distinct trajectory groups, with a mean BMI at age 20 of 19, 22 and 24 increasing to 23 (normal-to-normal), 29 (normal-to-overweight) and 37 (normal-to-obese) at 50-64 years of age, respectively. Women in the normal-to-obese trajectory group experienced significantly higher overall mortality than those in the normal-to-normal trajectory group (HR 1.76, 95% CI 1.21?2.56). The association declined to a non-significant level after adjustments for clinical prognostic factors. Although not significant, the same tendency was seen for breast cancer-specific mortality. The association was strongest in women with oestrogen receptor-negative tumours. Weight changes over time were not significantly different from a single BMI measure before diagnosis to predict survival. CONCLUSION: Weight gain affects overall mortality after breast cancer but clinical prognostic factors largely eliminate the association. Using trajectories of weight changes did not improve the predictive value compared to a single measure of BMI.

10.-
An estrogen-related lifestyle score is associated with risk of postmenopausal breast cancer in the PLCO cohort.
Guinter, M.A.; McLain, A.C.; Merchant, A.T.; Sandler, D.P.; Steck, S.E.
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Resumen:
PURPOSE: Healthy or unhealthy lifestyle behaviors are often adopted together. We aimed to investigate the combined effect of estrogen-related lifestyle factors on postmenopausal breast cancer risk. METHODS: Data from 27,153 women enrolled in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial were used. We created an estrogen-related lifestyle score (ERLS) by incorporating a previously developed measure of estrogenic diet, alcohol intake, body mass index (BMI), and physical activity. The scores ranged from 0 to 6 with alcohol and BMI accounting for higher weights than the other factors. To evaluate the preventive possibilities of a low estrogen-related lifestyle and to be consistent with other published lifestyle scores, higher scores were set to correspond with potentially lower estrogenic lifestyle. The association between the ERLS and incident breast cancer was examined using Cox proportional hazards models. RESULTS: Participants with an ERLS of 4 or = 5 had a 23% (HR 0.77; 95% CI 0.67-0.89) and 34% (HR 0.66; 95% CI 0.56-0.78) lower risk of breast cancer, respectively, compared to those with an ERLS = 2 after multivariable adjustment. Estimates were similar when restricting to invasive cases or estrogen receptor -positive subtypes. No single lifestyle component appeared to drive the association. CONCLUSIONS: Our findings suggest that the combined effect of a lifestyle characterized by a low estrogenic diet, low alcohol consumption, low body weight, and high levels of physical activity are associated with a reduction in postmenopausal breast cancer risk, possibly through an influence on estrogen metabolism.