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1
Subsequent Breast Cancer Risk Following Diagnosis of Atypical Ductal Hyperplasia on Needle Biopsy.
Menes, T.S.; Kerlikowske, K.; Lange, J.; Jaffer, S.; Rosenberg, R.; Miglioretti, D.L.
Vol. 3 Nr. 1 Página: 36 - 41 Fecha de publicación: 01/01/2017
Resumen:
Importance: Atypical ductal hyperplasia (ADH) is a known risk factor for breast cancer. Published risk estimates are based on cohorts that included women whose ADH was diagnosed before widespread use of screening mammograms and did not differentiate between the methods used to diagnose ADH, which may be related to the size of the ADH focus. These risks may overestimate the risk in women with presently diagnosed ADH. Objective: To examine the risk of invasive cancer associated with ADH diagnosed using core needle biopsy vs excisional biopsy. Design: A cohort study was conducted comparing the 10-year cumulative risk of invasive breast cancer in 955?331 women undergoing mammography with and without a diagnosis of ADH. Data were obtained from 5 breast imaging registries that participate in the National Cancer Institute-funded Breast Cancer Surveillance Consortium. Exposures: Diagnosis of ADH on core needle biopsy or excisional biopsy in women undergoing mammography. Main Outcomes and Measures: Ten-year cumulative risk of invasive breast cancer. Results: The sample included 955?331 women with 1727 diagnoses of ADH, 1058 (61.3%) of which were diagnosed by core biopsy and 635 (36.8%) by excisional biopsy. The mean (interquartile range) age of the women at diagnosis was 52.6 (46.9-60.4) years. From 1996 to 2012, the proportion of ADH diagnosed by core needle biopsy increased from 21% to 77%. Ten years following a diagnosis of ADH, the cumulative risk of invasive breast cancer was 2.6 (95% CI, 2.0-3.4) times higher than the risk in women with no ADH. Atypical ductal hyperplasia diagnosed via excisional biopsy was associated with an adjusted hazard ratio (HR) of 3.0 (95% CI, 2-4.5) and, via core needle biopsy, with an adjusted HR of 2.2 (95% CI, 1.5-3.4). Ten years after an ADH diagnosis, an estimated 5.7% (95% CI, 4.3%-10.1%) of the women had a diagnosis of invasive cancer. Women with ADH diagnosed on excisional biopsy had a slightly higher risk (6.7%; 95% CI, 3.0%-12.8%) compared with those with ADH diagnosed via core needle biopsy (5%; 95% CI, 2.2%-8.9%). Conclusions and Relevance: Current 10-year risks of invasive breast cancer after a diagnosis of ADH may be lower than those previously reported. The risk associated with ADH is slightly lower for women whose ADH was diagnosed by needle core biopsy compared with excisional biopsy.

2
Prognostic Factors for Local Control in Breast Cancer After Long-term Follow-up in the EORTC Boost vs No Boost Trial: A Randomized Clinical Trial.
Vrieling, C.; van Werkhoven, E.; Maingon, P.; Poortmans, P.; Weltens, C.; Fourquet, A.; Schinagl, D.; Oei, B.; Rodenhuis, C.C.; Horiot, J.C.; Struikmans, H.; Van Limbergen, E.; Kirova, Y.; Elkhuizen, P.; Bongartz, R.; Miralbell, R.; Morgan, D.A.; Dubois, J.B.; Remouchamps, V.; Mirimanoff, R.O.; Hart, G.; Collette, S.; Collette, L.; Bartelink, H.; European Organisation for Research and Treatment of Cancer, Radiation Oncology and Breast Cancer, G.r.oups.
Vol. 3 Nr. 1 Página: 42 - 48 Fecha de publicación: 01/01/2017
Resumen:
Importance: Prognostic factors of ipsilateral breast tumor recurrence (IBTR) may change over time following breast-conserving therapy. Objective: The EORTC "boost no boost" trial showed that young age and high-grade invasive carcinoma were the most important risk factors for IBTR. This study reanalyses pathological prognostic factors related to IBTR using long-term follow-up. Design, Setting, and Participants: Participants included 5569 early-stage breast cancer patients, treated with breast-conserving surgery (BCS) and whole-breast irradiation (WBI), who were randomized between no boost and a 16-Gy boost in the EORTC phase III "boost no boost" trial (1989-1996). A total of 1616 patients with a microscopically complete resection (according to local pathologists), included in the central pathology review, have been analyzed in this study. Median follow-up was 18.2 years. Interventions: No further treatment or 16-Gy boost, after BCS and 50-Gy WBI. Main Outcomes and Measures: Time to ipsilateral breast tumor recurrence (IBTR) as first event. Results: The 20-year cumulative incidence of IBTR in 1616 patients (160 events observed) was 15% (95% CI, 12%-17%). Young age (P < .001) and presence of ductal carcinoma in situ (DCIS) (HR, 2.15; 95% CI, 1.36-3.38; P = .001) were associated with an increased risk of IBTR in multivariable analysis. The cumulative incidence of IBTR at 20 years was 34% (95% CI, 25%-41%), 14% (95% CI, 10%-18%), and 11% (95% CI, 8%-15%), in patients 40 years or younger, 41 to 50 years and 50 years or older, respectively (P < .001). This incidence was 18% (95% CI, 14%-22%) and 9% (95% CI, 6%-12%) for tumors with and without DCIS (P < .001). High-grade tumors relapsed more frequently early during follow-up but the relative effect of age and presence of DCIS seemed stable over time. The boost reduced the 20-year IBTR incidence from 31% (95% CI, 22%-39%) to 15% (95% CI, 8%-21%) (HR, 0.37; 95% CI, 0.22-0.62; P < .001) in high-risk patients (=50 years with DCIS present). Conclusions and Relevance: The association of high-grade invasive tumor with IBTR diminished during follow-up, while the effect of DCIS adjacent to invasive tumor seemed to remain stable. Therefore, patients with high-grade invasive tumors should be monitored closely, especially in the first 5 years, while additional DCIS is an indication for longer follow-up, emphasizing the importance of long-term trial follow-up to estimate absolute effects accurately. Trial Registration: clinicaltrials.gov Identifier: NCT02295033.

3
Association of Regional Intensity of Ductal Carcinoma In Situ Treatment With Likelihood of Breast Preservation.
Punglia, R.S.; Cronin, A.M.; Uno, H.; Stout, N.K.; Ozanne, E.M.; Greenberg, C.C.; Frank, E.S.; Schrag, D.
Vol. 3 Nr. 1 Página: 101 - 104 Fecha de publicación: 01/01/2017
Resumen:
Importance: Large regional variation exists in the use of radiotherapy after breast-conserving surgery (BCS) for ductal carcinoma in situ (DCIS). Although patients who do not receive initial radiotherapy for DCIS are candidates for subsequent BCS if they experience a second breast event, many undergo mastectomy instead. Objective: To examine whether regional practice patterns of radiotherapy for DCIS affect the use of mastectomy in these patients. Design, Setting, and Participants: A retrospective analysis of population-based databases (Surveillance, Epidemiology, and End Results [SEER] and SEER-Medicare). Data were obtained for 2679 women in SEER with a diagnosis of DCIS between 1990 and 2011 and for 757 women in SEER-Medicare with a DCIS diagnosis between 1991 and 2009 who had not undergone radiotherapy for DCIS and experienced a subsequent breast cancer or DCIS diagnosis. Exposures: Treatment intensity for primary DCIS (high, medium, low), as defined by separating health service areas (HSAs) into 3 clusters based on radiotherapy use. Main Outcomes and Measures: Mastectomy vs BCS at a second breast event defined as DCIS recurrence or new invasive cancer. Results: The median (SD) ages of the participants was 64 (13) years for the 2679 SEER population and 79 (6) years for the SEER-Medicare cohort. Residence in an HSA characterized by greater radiotherapy use for DCIS increased the likelihood of receiving mastectomy vs BCS at a subsequent breast event, even among women who had not previously received radiotherapy for DCIS. Adjusted odds ratios for receiving mastectomy were 1.43 (95% CI, 1.10-1.85) and 1.90 (95% CI, 1.27-2.84) in SEER and SEER-Medicare databases, respectively, among women residing in an HSA with the greatest radiotherapy use vs the least, corresponding to an adjusted increase from 40.8% to 49.6%, and from 38.6% to 54.5%. Conclusions and Relevance: Areas with more radiotherapy use for DCIS had increased use of mastectomy at the time of a second breast event even among patients eligible for breast conservation. This association suggests that physician-related factors are affecting the likelihood of breast preservation.

4
Effect of a Patient-Centered Communication Intervention on Oncologist-Patient Communication, Quality of Life, and Health Care Utilization in Advanced Cancer: The VOICE Randomized Clinical Trial.
Epstein, R.M.; Duberstein, P.R.; Fenton, J.J.; Fiscella, K.; Hoerger, M.; Tancredi, D.J.; Xing, G.; Gramling, R.; Mohile, S.; Franks, P.; Kaesberg, P.; Plumb, S.; Cipri, C.S.; Street RL, ; Shields, C.G.; Back, A.L.; Butow, P.; Walczak, A.; Tattersall, M.; Venuti, A.; Sullivan, P.; Robinson, M.; Hoh, B.; Lewis, L.; Kravitz, R.L.
Vol. 3 Nr. 1 Página: 92 - 100 Fecha de publicación: 01/01/2017
Resumen:
Importance: Observational studies demonstrate links between patient-centered communication, quality of life (QOL), and aggressive treatments in advanced cancer, yet few randomized clinical trials (RCTs) of communication interventions have been reported. Objective: To determine whether a combined intervention involving oncologists, patients with advanced cancer, and caregivers would promote patient-centered communication, and to estimate intervention effects on shared understanding, patient-physician relationships, QOL, and aggressive treatments in the last 30 days of life. Design, Setting, and Participants: Cluster RCT at community- and hospital-based cancer clinics in Western New York and Northern California; 38 medical oncologists (mean age 44.6 years; 11 (29%) female) and 265 community-dwelling adult patients with advanced nonhematologic cancer participated (mean age, 64.4 years, 146 [55.0%] female, 235 [89%] white; enrolled August 2012 to June 2014; followed for 3 years); 194 patients had participating caregivers. Interventions: Oncologists received individualized communication training using standardized patient instructors while patients received question prompt lists and individualized communication coaching to identify issues to address during an upcoming oncologist visit. Both interventions focused on engaging patients in consultations, responding to emotions, informing patients about prognosis and treatment choices, and balanced framing of information. Control participants received no training. Main Outcomes and Measures: The prespecified primary outcome was a composite measure of patient-centered communication coded from audio recordings of the first oncologist visit following patient coaching (intervention group) or enrollment (control). Secondary outcomes included the patient-physician relationship, shared understanding of prognosis, QOL, and aggressive treatments and hospice use in the last 30 days of life. Results: Data from 38 oncologists (19 randomized to intervention) and 265 patients (130 intervention) were analyzed. In fully adjusted models, the intervention resulted in clinically and statistically significant improvements in the primary physician-patient communication end point (adjusted intervention effect, 0.34; 95% CI, 0.06-0.62; P = .02). Differences in secondary outcomes were not statistically significant. Conclusions and Relevance: A combined intervention that included oncologist communication training and coaching for patients with advanced cancer was effective in improving patient-centered communication but did not affect secondary outcomes. Trial Registration: clinicaltrials.gov Identifier: NCT01485627.

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Neoadjuvant Endocrine Therapy for Estrogen Receptor-Positive Breast Cancer: A Systematic Review and Meta-analysis.
Spring, L.M.; Gupta, A.; Reynolds, K.L.; Gadd, M.A.; Ellisen, L.W.; Isakoff, S.J.; Moy, B.; Bardia, A.
Vol. 2 Nr. 11 Página: 1477 - 1486 Fecha de publicación: 01/11/2016
Resumen:
Importance: Estrogen receptor-positive (ER+) tumors of the breast are generally highly responsive to endocrine treatment. Although endocrine therapy is the mainstay of adjuvant treatment for ER+ breast cancer, the role of endocrine therapy in the neoadjuvant setting is unclear. Objective: To evaluate the effect of neoadjuvant endocrine therapy (NET) on the response rate and the rate of breast conservation surgery (BCS) for ER+ breast cancer. Data Sources: Based on PRISMA guidelines, a librarian-led search of PubMed and Ovid MEDLINE was performed to identify eligible trials published from inception to May 15, 2015. The search was performed in May 2015. Study Selection: Inclusion criteria were prospective, randomized, neoadjuvant clinical trials that reported response rates with at least 1 arm incorporating NET (n = 20). Two authors independently analyzed the studies for inclusion. Data Extraction and Synthesis: Pooled odds ratios (ORs), 95% CIs, and P values were estimated for end points using the fixed- and random-effects statistical model. Results: The analysis included 20 studies with 3490 unique patients. Compared with combination chemotherapy, NET as monotherapy with aromatase inhibitors had a similar clinical response rate (OR, 1.08; 95% CI, 0.50-2.35; P = .85; n = 378), radiological response rate (OR, 1.38; 95% CI, 0.92-2.07; P = .12; n = 378), and BCS rate (OR, 0.65; 95% CI, 0.41-1.03; P = .07; n = 334) but with lower toxicity. Aromatase inhibitors were associated with a significantly higher clinical response rate (OR, 1.69; 95% CI, 1.36-2.10; P < .001; n = 1352), radiological response rate (OR, 1.49; 95% CI, 1.18-1.89; P < .001; n = 1418), and BCS rate (OR, 1.62; 95% CI, 1.24-2.12; P < .001; n = 918) compared with tamoxifen. Dual combination therapy with growth factor pathway inhibitors was associated with a higher radiological response rate (OR, 1.59; 95% CI, 1.04-2.43; P = .03; n = 355), but not clinical response rate (OR, 0.76; 95% CI, 0.54-1.07; P = .11; n = 537), compared with endocrine monotherapy. The incidence of pathologic complete response was low (<10%). Conclusions and Relevance: Neoadjuvant endocrine therapy, even as monotherapy, is associated with similar response rates as neoadjuvant combination chemotherapy but with significantly lower toxicity, suggesting that NET needs to be reconsidered as a potential option in the appropriate setting. Additional research is needed to develop rational NET combinations and predictive biomarkers to personalize the optimal neoadjuvant strategy for ER+ breast cancer.

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Breast Cancer Risk From Modifiable and Nonmodifiable Risk Factors Among White Women in the United States.
Maas, P.; Barrdahl, M.; Joshi, A.D.; Auer, P.L.; Gaudet, M.M.; Milne, R.L.; Schumacher, F.R.; Anderson, W.F.; Check, D.; Chattopadhyay, S.; Baglietto, L.; Berg, C.D.; Chanock, S.J.; Cox, D.G.; Figueroa, J.D.; Gail, M.H.; Graubard, B.I.; Haiman, C.A.; Hankinson, S.E.; Hoover, R.N.; Isaacs, C.; Kolonel, L.N.; Le Marchand, L.; Lee, I.M.; Lindström, S.; Overvad, K.; Romieu, I.; Sanchez, M.J.; Southey, M.C.; Stram, D.O.; Tumino, R.; VanderWeele, T.J.; Willett, W.C.; Zhang, S.; Buring, J.E.; Canzian,
Vol. 2 Nr. 10 Página: 1295 - 1302 Fecha de publicación: 01/10/2016
Resumen:
Importance: An improved model for risk stratification can be useful for guiding public health strategies of breast cancer prevention. Objective: To evaluate combined risk stratification utility of common low penetrant single nucleotide polymorphisms (SNPs) and epidemiologic risk factors. Design, Setting, and Participants: Using a total of 17?171 cases and 19?862 controls sampled from the Breast and Prostate Cancer Cohort Consortium (BPC3) and 5879 women participating in the 2010 National Health Interview Survey, a model for predicting absolute risk of breast cancer was developed combining information on individual level data on epidemiologic risk factors and 24 genotyped SNPs from prospective cohort studies, published estimate of odds ratios for 68 additional SNPs, population incidence rate from the National Cancer Institute-Surveillance, Epidemiology, and End Results Program cancer registry and data on risk factor distribution from nationally representative health survey. The model is used to project the distribution of absolute risk for the population of white women in the United States after adjustment for competing cause of mortality. Exposures: Single nucleotide polymorphisms, family history, anthropometric factors, menstrual and/or reproductive factors, and lifestyle factors. Main Outcomes and Measures: Degree of stratification of absolute risk owing to nonmodifiable (SNPs, family history, height, and some components of menstrual and/or reproductive history) and modifiable factors (body mass index [BMI; calculated as weight in kilograms divided by height in meters squared], menopausal hormone therapy [MHT], alcohol, and smoking). Results: The average absolute risk for a 30-year-old white woman in the United States developing invasive breast cancer by age 80 years is 11.3%. A model that includes all risk factors provided a range of average absolute risk from 4.4% to 23.5% for women in the bottom and top deciles of the risk distribution, respectively. For women who were at the lowest and highest deciles of nonmodifiable risks, the 5th and 95th percentile range of the risk distribution associated with 4 modifiable factors was 2.9% to 5.0% and 15.5% to 25.0%, respectively. For women in the highest decile of risk owing to nonmodifiable factors, those who had low BMI, did not drink or smoke, and did not use MHT had risks comparable to an average woman in the general population. Conclusions and Relevance: This model for absolute risk of breast cancer including SNPs can provide stratification for the population of white women in the United States. The model can also identify subsets of the population at an elevated risk that would benefit most from risk-reduction strategies based on altering modifiable factors. The effectiveness of this model for individual risk communication needs further investigation.

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JAMA Oncology
Prevalence of ESR1 Mutations in Cell-Free DNA and Outcomes in Metastatic Breast Cancer: A Secondary Analysis of the BOLERO-2 Clinical Trial.
Chandarlapaty, S.; Chen, D.; He, W.; Sung, P.; Samoila, A.; You, D.; Bhatt, T.; Patel, P.; Voi, M.; Gnant, M.; Hortobagyi, G.; Baselga, J.; Moynahan, M.E.
Vol. 2 Nr. 10 Página: 1310 - 1315 Fecha de publicación: 01/10/2016
Resumen:
Importance: Estrogen receptor a (ESR1) mutations found in metastatic breast cancer (MBC) promote ligand-independent receptor activation and resistance to estrogen-deprivation therapy in laboratory models. The prevalence of these mutations and their potential impact on clinical outcomes has not been established. Objective: To determine the prevalence of ESR1 mutations (Y537S and D538G) in estrogen receptor (ER)-positive MBC and determine whether mutation is associated with inferior outcomes. Design, Setting, and Participants: From December 16, 2014, to August 26, 2015, we analyzed cell-free DNA (cfDNA) from baseline plasma samples from participants in the BOLERO-2 double-blind phase 3 study that randomized patients from 189 centers in 24 countries with MBC to exemestane plus placebo or exemestane plus everolimus. The study enrolled postmenopausal women with a diagnosis of MBC and prior exposure to an aromatase inhibitor. Baseline plasma samples were available from 541 of 724 patients (74.7%). We assessed the effect of mutation on overall survival of the population and the effect of mutation on progression-free survival (PFS) by treatment arm. Interventions: Patients were randomized to treatment with exemestane (25 mg oral daily) together with everolimus (10 mg oral daily) or with placebo. Main Outcomes and Measures: The 2 most frequent mutations in ESR1 (Y537S and D538G) were analyzed from cfDNA using droplet digital polymerase chain reaction and samples scored as wild-type, D538G, Y537S, or double mutant. Cox-proportional hazards model was used to assess PFS in patient subgroups defined by mutations, and the effect of each mutation on overall survival. Results: Of 541 evaluable patients, 156 (28.8%) had ESR1 mutation D538G (21.1%) and/or Y537S (13.3%), and 30 had both. These mutations were associated with shorter overall survival (wild-type, 32.1 months [95% CI, 28.09-36.40 months]; D538G, 25.99 months [95% CI, 19.19-32.36 months]; Y537S, 19.98 months [13.01-29.31 months]; both mutations, 15.15 months [95% CI, 10.87-27.43 months]). The D538G group (hazard ratio, 0.34 [95% CI, 0.02-0.57]) derived a similar PFS benefit as wild type from addition of everolimus to exemestane. Conclusions and Relevance: ESR1 mutations are prevalent in ER-positive aromatase inhibitor-treated MBC. Both Y537S and D538G mutations are associated with more aggressive disease biology. Trial Registration: clinicaltrials.gov Identifier: NCT00863655.

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Nonadherence to Medications for Chronic Conditions and Nonadherence to Adjuvant Hormonal Therapy in Women With Breast Cancer.
Neugut, A.I.; Zhong, X.; Wright, J.D.; Accordino, M.; Yang, J.; Hershman, D.L.
Vol. 2 Nr. 10 Página: 1326 - 1332 Fecha de publicación: 01/10/2016
Resumen:
Importance: While adjuvant hormonal therapy (HT) reduces mortality for women with nonmetastatic breast cancer, nonadherence to HT is common. Objective: We investigated the association between patterns of prior nonadherence to medications for chronic conditions with HT nonadherence. Design, Setting, and Participants: For this retrospective cohort study, the MarketScan database was scanned for women 18 years and older who had been diagnosed with nonmetastatic breast cancer between January 1, 2010, and December 31, 2012, and who filled 2 or more prescriptions for tamoxifen and/or an aromatase inhibitor. Main Exposures and Outcomes: Nonadherence to medications for 6 chronic conditions (hypertension, hyperlipidemia, gastroesophageal reflux disease, thyroid disease, diabetes, osteoporosis) in the 12 months before diagnosis was defined as a medication possession ratio (MPR) less than 80%. Nonadherence to HT was defined as an MPR less than 80% between the first and last prescription for HT up to 2 years. Analysis: Multivariable logistic regression was used to determine the association between prior medication nonadherence and HT nonadherence. Results: Of 21?255 women treated with adjuvant HT, 3314 (15.6%) were nonadherent, and age (<55 or =75 years vs 55-64 years), higher 30-day out-of-pocket costs, and increased comorbidities were associated with nonadherence. Women without prior medications for 1 of the chronic conditions (n = 7828 [37%]) had an 18.4% nonadherence rate to HT. Those who used 1 or more medication prior to HT and were adherent (n = 9223 [43%]) had a 9.8% nonadherence rate to HT (relative to those without prior medications: odds ratio [OR] 0.56; 95% CI, 0.50-0.61), while those who were nonadherent to their chronic medications (n = 4214 [20%]) had a 23.1% nonadherence rate to HT (OR 1.43; 95% CI, 1.30-1.58). Adherence and nonadherence for medications for each of the 6 medical conditions was associated with adherence or nonadherence for HT, respectively. Conclusions and Relevance: We found that nonadherence to medications for chronic conditions prior to HT was associated with greater nonadherence to oral HT in patients with breast cancer. Medication nonadherence history may play an important role in determining patients at risk for nonadherence to a subsequent medication for a different illness, such as HT, and a potential target for future interventions.

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Variation in the Incidence and Magnitude of Tumor-Infiltrating Lymphocytes in Breast Cancer Subtypes: A Systematic Review.
Stanton, S.E.; Adams, S.; Disis, M.L.
Vol. 2 Nr. 10 Página: 1354 - 1360 Fecha de publicación: 01/10/2016
Resumen:
Importance: The presence of tumor-infiltrating lymphocytes (TILs) is a favorable prognostic factor in breast cancer, and TILs may synergize with chemotherapy and immune checkpoint inhibitor therapy for improved clinical response. A more detailed understanding of the variation in lymphocytic infiltration in breast cancer may aid in identifying subtypes more amenable to immunomodulation. Objective: To determine the median percentage of patients with breast cancer with no, intermediate, or high levels of TIL and assess variations in lymphocytic cell subsets across breast cancer subtypes. Evidence Review: Eligible studies (PubMed, 1990-2015) analyzed tumor lymphocytic, CD8+, and FOXP3+ cellular infiltrates, and used multivariable analyses and quantitative methods for enumerating cell populations. Selection of of studies was performed in accordance with PRISMA guidelines and evaluated by 2 independent appraisers. Findings: Fifteen studies (n = 13?914) met prespecified criteria and were reviewed in December 2015. A median of 11% (range, 5%-26%) of breast cancers demonstrate lymphocyte-predominant breast cancer (LPBC), with approximately 16% of cancers showing no evidence of TILs. Triple-negative (TN) breast cancers demonstrated the highest incidence of LPBC (20%; range, 4%-37%). This incidence is similar to that of breast cancers that are human epidermal growth factor 2 positive and either hormone receptor positive or negative (HER2+) at 16% (range 11%-24%). Hormone receptor positive/HER2- (HR+) breast cancer showed the lowest incidence of LPBC at 6% (range, 3%-12%). CD8+ T-cell infiltrates, indicative of type I immunity, were found in 48% of all breast cancers (range, 32%-80%) with similar levels observed in TN (60%; range, 40%-91%) and HER2+ disease (61%; range, 40%-83%). Fewer HR+ tumors demonstrated CD8+ TIL (43%; range, 30%-73%). The highest levels of FOXP3+ cells were observed in TN (70%; range, 65%-76%) and HER2+ disease (67%; range, 61%-74%). A minority of HR+ breast cancers demonstrated high levels of tumor-infiltrating FOXP3+ cells (38%; range, 35%-41%). Conclusions and Relevance: The magnitude of TIL is variable within and between breast cancer subtypes. Levels of lymphocytic subpopulations may identify breast cancers more amenable to immunomodulation and indicate additional strategies to enhance immunity in patients with low to moderate levels of TILs.

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Association Between Complementary and Alternative Medicine Use and Breast Cancer Chemotherapy Initiation: The Breast Cancer Quality of Care (BQUAL) Study.
Greenlee, H.; Neugut, A.I.; Falci, L.; Hillyer, G.C.; Buono, D.; Mandelblatt, J.S.; Roh, J.M.; Ergas, I.J.; Kwan, M.L.; Lee, M.; Tsai, W.Y.; Shi, Z.; Lamerato, L.; Kushi, L.H.; Hershman, D.L.
Vol. 2 Nr. 9 Página: 1170 - 6 Fecha de publicación: 01/09/2016
Resumen:
IMPORTANCE: Not all women initiate clinically indicated breast cancer adjuvant treatment. It is important for clinicians to identify women at risk for noninitiation. OBJECTIVE: To determine whether complementary and alternative medicine (CAM) use is associated with decreased breast cancer chemotherapy initiation. DESIGN, SETTING, AND PARTICIPANTS: In this multisite prospective cohort study (the Breast Cancer Quality of Care [BQUAL] study) designed to examine predictors of breast cancer treatment initiation and adherence, 685 women younger than 70 years with nonmetastatic invasive breast cancer were recruited from Columbia University Medical Center, Kaiser Permanente Northern California, and Henry Ford Health System and enrolled between May 2006 and July 31, 2010. Overall, 306 patients (45%) were clinically indicated to receive chemotherapy per National Comprehensive Cancer Network guidelines. Participants were followed for up to 12 months. EXPOSURES: Baseline interviews assessed current use of 5 CAM modalities (vitamins and/or minerals, herbs and/or botanicals, other natural products, mind-body self-practice, mind-body practitioner-based practice). CAM use definitions included any use, dietary supplement use, mind-body use, and a CAM index summing the 5 modalities. MAIN OUTCOMES AND MEASURES: Chemotherapy initiation was assessed via self-report up to 12 months after baseline. Multivariable logistic regression models examined a priori hypotheses testing whether CAM use was associated with chemotherapy initiation, adjusting for demographic and clinical covariates, and delineating groups by age and chemotherapy indication. RESULTS: A cohort of 685 women younger than 70 years (mean age, 59 years; median age, 59 years) with nonmetastatic invasive breast cancer were recruited and followed for up to 12 months to examine predictors of breast cancer treatment initiation. Baseline CAM use was reported by 598 women (87%). Chemotherapy was initiated by 272 women (89%) for whom chemotherapy was indicated, compared with 135 women (36%) for whom chemotherapy was discretionary. Among women for whom chemotherapy was indicated, dietary supplement users and women with high CAM index scores were less likely than nonusers to initiate chemotherapy (odds ratio [OR], 0.16; 95% CI, 0.03-0.51; and OR per unit, 0.64; 95% CI, 0.46-0.87, respectively). Use of mind-body practices was not related to chemotherapy initiation (OR, 1.45; 95% CI, 0.57-3.59). There was no association between CAM use and chemotherapy initiation among women for whom chemotherapy was discretionary. CONCLUSIONS AND RELEVANCE: CAM use was high among patients with early-stage breast cancer enrolled in a multisite prospective cohort study. Current dietary supplement use and higher number of CAM modalities used but not mind-body practices were associated with decreased initiation of clinically indicated chemotherapy. Oncologists should consider discussing CAM with their patients during the chemotherapy decision-making process.

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Clinical Diagnosis of Mental Disorders Immediately Before and After Cancer Diagnosis: A Nationwide Matched Cohort Study in Sweden.
Lu, D.; Andersson, T.M.; Fall, K.; Hultman, C.M.; Czene, K.; Valdimarsdóttir, U.; Fang, F.
Vol. 2 Nr. 9 Página: 1188 - 96 Fecha de publicación: 01/09/2016
Resumen:
IMPORTANCE: Psychiatric comorbidities are common among patients with cancer. However, whether or not there is increased risk of mental disorders during the diagnostic workup leading to a cancer diagnosis was unknown. OBJECTIVE: To examine the relative risks of depression, anxiety, substance abuse, somatoform/conversion disorder, and stress reaction/adjustment disorder during the periods before and after cancer diagnosis compared with individuals without cancer. DESIGN, SETTING, AND PARTICIPANTS: Nationwide matched cohort study from January 1, 2001, to December 31, 2010, in a Swedish population and health registers. MAIN OUTCOMES AND MEASURES: We estimated the time-varying hazard ratios (HRs) of the first clinical diagnosis of the studied mental disorders from 2 years before cancer diagnosis, through the time of diagnosis, and until 10 years after diagnosis, adjusting for age, sex, calendar period, and educational level. To assess milder mental conditions and symptoms, we further assessed the use of related psychiatric medications for patients with cancer diagnosed during 2008-2009. RESULTS: The study included 304?118 patients with cancer and 3?041?174 cancer-free individuals who were randomly selected from the Swedish population and individually matched to the patients with cancer on year of birth and sex. The median age at diagnosis for the patients with cancer was 69 years, and 46.9% of the patients were female. The relative rate for all studied mental disorders started to increase from 10 months before cancer diagnosis (HR, 1.1; 95% CI, 1.1-1.2), peaked during the first week after diagnosis (HR, 6.7; 95% CI, 6.1-7.4), and decreased rapidly thereafter but remained elevated 10 years after diagnosis (HR, 1.1; 95% CI, 1.1-1.2). The rate elevation was clear for all main cancers except nonmelanoma skin cancer and was stronger for cancers of poorer prognosis. Compared with cancer-free individuals, increased use of psychiatric medications was noted from 1 month before cancer diagnosis and peaked around 3 months after diagnosis among patients with cancer. CONCLUSIONS AND RELEVANCE: Patients diagnosed as having cancer had increased risks of several common mental disorders from the year before diagnosis. These findings support the existing guidelines of integrating psychological management into cancer care and further call for extended vigilance for multiple mental disorders starting from the time of the cancer diagnostic workup.

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Angiotensin II-Receptor Inhibition With Candesartan to Prevent Trastuzumab-Related Cardiotoxic Effects in Patients With Early Breast Cancer: A Randomized Clinical Trial.
Boekhout, A.H.; Gietema, J.A.; Milojkovic Kerklaan, B.; van Werkhoven, E.D.; Altena, R.; Honkoop, A.; Los, M.; Smit, W.M.; Nieboer, P.; Smorenburg, C.H.; Mandigers, C.M.; van der Wouw,

A.J.; Kessels, L.; van der Velden, A.W.; Ottevanger, P.B.; Smilde, T.; de Boer, J.; van Veldhuisen, D.J.; Kema, I.P.; de Vries, E.G.; Schellens, J.H.
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Resumen:
IMPORTANCE: This is the first randomized placebo-controlled evaluation of a medical intervention for the prevention of trastuzumab-related cardiotoxic effects. OBJECTIVE: To determine as the primary end point whether angiotensin II antagonist treatment with candesartan can prevent or ameliorate trastuzumab-related cardiotoxic effects, defined as a decline in left ventricular ejection fraction (LVEF) of more than 15% or a decrease below the absolute value 45%. DESIGN: This randomized, placebo-controlled clinical study was conducted between October 2007 and October 2011 in 19 hospitals in the Netherlands, enrolling 210 women with early breast cancer testing positive for human epidermal growth factor receptor 2 (HER2) who were being considered for adjuvant systemic treatment with anthracycline-containing chemotherapy followed by trastuzumab. INTERVENTIONS: A total of 78 weeks of candesartan (32 mg/d) or placebo treatment; study treatment started at the same day as the first trastuzumab administration and continued until 26 weeks after completion of trastuzumab treatment. MAIN OUTCOMES AND MEASURES: The primary outcome was LVEF. Secondary end points included whether the N-terminal of the prohormone brain natriuretic peptide (NT-proBNP) and high-sensitivity troponin T (hs-TnT) can be used as surrogate markers and whether genetic variability in germline ERBB2 (formerly HER2 or HER2/neu) correlates with trastuzumab-related cardiotoxic effects. RESULTS: A total of 206 participants were evaluable (mean age, 49 years; age range, 25-69 years) 103 in the candesartan group (mean age, 50 years; age range, 25-69 years) and 103 in the placebo group (mean age, 50 years; age range, 30-67 years). Of these, 36 manifested at least 1 of the 2 primary cardiac end points. There were 3.8% more cardiac events in the candesartan group than in the placebo group (95% CI, -7% to 15%; P = .58): 20 events (19%) and 16 events (16%), respectively. The 2-year cumulative incidence of cardiac events was 0.28 (95% CI, 0.13-0.40) in the candesartan group and 0.16 (95% CI, 0.08-0.22) in the placebo group (P = .56). Candesartan did not affect changes in NT-proBNP and hs-TnT values, and these biomarkers were not associated with significant changes in LVEF. The Ala1170Pro homozygous ERBB2 genotype was associated with a lower likelihood of the occurrence of a cardiac event compared with Pro/Pro + Ala/Pro genotypes in multivariate analysis (odds ratio, 0.09; 95% CI, 0.02-0.45; P = .003). CONCLUSIONS AND RELEVANCE: The findings do not support the hypothesis that concomitant use of candesartan protects against a decrease in left ventricular ejection fraction during or shortly after trastuzumab treatment in early breast cancer. The ERBB2 germline Ala1170Pro single nucleotide polymorphism may be used to identify patients who are at increased risk of trastuzumab-related cardiotoxic effects. TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT00459771.

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