Publicaciones Seleccionadas Mayo 2018

MASTOLOGIA

Aporte Dres Lorusso & Foderé

Solo Información Médica

Volumen 3 Nro 2

BREAST CANCER RESEARCH AND TREATMENT

1
Is invasion a necessary step for metastases in breast cancer?
Narod, S.A.; Sopik, V.
Vol. 169 Nr. 1 Página: 9 - 23 Fecha de publicación: 01/05/2018
Resumen:
PURPOSE: To review the empirical evidence to support the conventional (sequential) model of breast cancer progression, which is based on the paradigm that cancer passes through several stages, including an in situ stage prior to an invasive stage, and thereafter (in some cases) disseminates to the lymph nodes and distant organs. METHODS: We review the cancer literature of the last 50 years which relates to the prevention of invasive breast cancer (through radiotherapy or surgery) and reductions in the mortality for breast cancer. RESULTS: For both invasive cancers and DCIS, the literature indicates that prevention of in-breast invasive recurrences does not prevent death from breast cancer. Moreover, the presence of residual cancer cells in the breast after breast-conserving surgery does not compromise the cure rate. CONCLUSION: We propose an alternate (parallel) model of breast cancer wherein there is a small pool of cancer stem cells which have metastatic potential from their inception and which disseminate synchronously through several routes-to the breast stroma, to the lymph nodes and to distant organs. Cancer cells which disseminate to the breast give rise to cells which make up the bulk of the tumour mass but these are not the source of the distant metastases.

2
Digital image analysis of Ki67 proliferation index in breast cancer using virtual dual staining on whole tissue sections: clinical validation and inter-platform agreement.
Koopman, T.; Buikema, H.J.; Hollema, H.; de Bock, G.H.; van der Vegt, B.
Vol. 169 Nr. 1 Página: 33 - 42 Fecha de publicación: 01/05/2018
Resumen:
PURPOSE: The Ki67 proliferation index is a prognostic and predictive marker in breast cancer. Manual scoring is prone to inter- and intra-observer variability. The aims of this study were to clinically validate digital image analysis (DIA) of Ki67 using virtual dual staining (VDS) on whole tissue sections and to assess inter-platform agreement between two independent DIA platforms. METHODS: Serial whole tissue sections of 154 consecutive invasive breast carcinomas were stained for Ki67 and cytokeratin 8/18 with immunohistochemistry in a clinical setting. Ki67 proliferation index was determined using two independent DIA platforms, implementing VDS to identify tumor tissue. Manual Ki67 score was determined using a standardized manual counting protocol. Inter-observer agreement between manual and DIA scores and inter-platform agreement between both DIA platforms were determined and calculated using Spearman's correlation coefficients. Correlations and agreement were assessed with scatterplots and Bland-Altman plots. RESULTS: Spearman's correlation coefficients were 0.94 ($p < 0.001$) for inter-observer agreement between manual counting and platform A, 0.93 ($p < 0.001$) between manual counting and platform B, and 0.96 ($p < 0.001$) for inter-platform agreement. Scatterplots and Bland-Altman plots revealed no skewness within specific data ranges. In the few cases with = 10% difference between manual counting and DIA, results by both platforms were similar. CONCLUSIONS: DIA using VDS is an accurate method to determine the Ki67 proliferation index in breast cancer, as an alternative to manual scoring of whole sections in clinical practice. Inter-platform agreement between two different DIA platforms was excellent, suggesting vendor-independent clinical implementability.

3
Impact of an embedded genetic counselor on breast cancer treatment.
Pederson, H.J.; Hussain, N.; Noss, R.; Yanda, C.; O'Rourke, C.; Eng, C.; Grobmyer, S.R.
Vol. 169 Nr. 1 Página: 43 - 46 Fecha de publicación: 01/05/2018
Resumen:
BACKGROUND: We predicted that embedding a genetic counselor within our breast practice would improve identification of high-risk individuals, timeliness of care, and appropriateness of surgical decision making. The aim of this study is to compare cancer care between 2012 and 2014, prior to embedding a genetic counselor in the breast center and following the intervention, respectively. METHODS: A retrospective review of patients diagnosed with breast cancer in 2012 ($n = 471$) and 2014 ($n = 440$) was performed to assess patterns of medical genetics referral, compliance with referral, genetic testing findings, and impact on treatment. RESULTS: Between 2012 and 2014, patients were 49% more likely to be referred to genetics, 66% more likely to follow through with their genetic counseling appointment, experienced a 73% reduction in wait times to genetic counseling visits and 69% more likely to have genetic testing results prior to surgery. Notably, while the number of genetic mutations identified was in the expected range over both time periods (9% of those tested in 2012 vs. 6.6% of those tested in 2014), there was a 31% reduction in time to treatment in 2014 vs. 2012. CONCLUSION: Awareness of germline genetic mutations is critical in surgical decision making for newly diagnosed breast cancer patients. Having an experienced genetics specialist on site in a busy surgical breast clinic allows for timely access to genetic counseling and testing, and may have influenced time to treatment in our institution.

4
The PPAR? agonist efatutazone delays invasive progression and induces differentiation of ductal carcinoma in situ.
Ory, V.; Kietzman, W.B.; Boeckelman, J.; Kallakury, B.V.; Wellstein, A.; Furth, P.A.; Riegel, A.T.
Vol. 169 Nr. 1 Página: 47 - 57 Fecha de publicación: 01/05/2018
Resumen:
PURPOSE: Ductal carcinoma in situ (DCIS) is a pre-invasive lesion of the breast considered a precursor of invasive ductal carcinoma. This study aimed to determine whether activated PPAR? acts as a tumor suppressor in human DCIS progression. METHODS: We utilized the high-affinity PPAR? agonist, efatutazone, to activate endogenous PPAR? in a well-defined model for the progression of basal (triple negative) DCIS, MCFDCIS cells, cultured under 2D and 3D conditions. We studied the effects of activated PPAR? on DCIS progression in MCFDCIS xenograft and C3 (1)/Tag transgenic mice treated with 30 mg/kg of efatutazone. RESULTS: In vitro, efatutazone did not alter the MCFDCIS cell proliferation but induced phenotypic and gene expression changes, indicating that activated PPAR? is able to differentiate MCFDCIS cells into more luminal and lactational-like cells. In addition, MCFDCIS tumorsphere formation in 3D was reduced by PPAR? activation. In vivo, efatutazone-treated MCFDCIS tumors exhibited fat deposition along with upregulation of PPAR? responsive genes in both epithelial and stromal compartments, suggesting features of milk-producing mammary epithelial cell differentiation. The efatutazone-treated lesions were less invasive with fewer CD44+/p63+ basal progenitor cells. PPAR? activation downregulated Akt phosphorylation in these tumors, although the ERK pathway remained unchanged. Similar trends in gene expression changes consistent with lactational and luminal cell differentiation were observed in the C3(1)/Tag mouse model after efatutazone treatment. CONCLUSIONS: Our data suggest that activation of the PPAR? pathway differentiates DCIS lesions and may be a useful approach to delay DCIS progression.

5
Associations of coffee consumption and caffeine intake with mammographic breast density.
Yaghjyan, L.; Colditz, G.; Rosner, B.; Gasparova, A.; Tamimi, R.M.
Vol. 169 Nr. 1 Página: 115 - 123 Fecha de publicación: 01/05/2018
Resumen:
PURPOSE: Previous studies suggest that coffee and caffeine intake may be associated with reduced breast cancer risk. We investigated the association of coffee and caffeine intake with mammographic breast density by woman's menopausal status and, in postmenopausal women, by hormone therapy (HT). METHODS: This study included 4130 cancer-free women within the Nurses' Health Study and Nurses' Health Study II cohorts. Percent breast density (PD) was measured from digitized film mammograms using a computer-assisted thresholding technique and square root-transformed for the analysis. Average cumulative coffee/caffeine consumption was calculated using data from all food frequency questionnaires preceding the mammogram date. Information regarding breast cancer risk factors was obtained from questionnaires closest to the mammogram date. We used generalized linear regression to quantify associations of regular, decaffeinated, and total coffee, and energy-adjusted caffeine intake with percent density. RESULTS: In multivariable analyses, decaffeinated coffee was positively associated with PD in premenopausal women (2+ cups/day: ß = 0.23, p trend = 0.03). In postmenopausal women, decaffeinated and total coffee were inversely associated with PD (decaffeinated 2+ cups/day: ß = - 0.24, p trend = 0.04; total 4+ cups/day: ß = - 0.16, p trend = 0.02). Interaction of decaffeinated coffee with menopausal status was significant (p-interaction < 0.001). Among current HT users, regular coffee and caffeine were inversely associated with PD (regular coffee 4+ cups/day: ß = - 0.29, p trend = 0.01; caffeine 4th vs. 1st quartile: ß = - 0.32, p trend = 0.01). Among past users, decaffeinated coffee was inversely associated with PD (2+ cups/day ß = - 0.70, p trend = 0.02). CONCLUSIONS: Associations of decaffeinated coffee with percent density differ by woman's menopausal status. Associations of regular coffee and caffeine with percent density may differ by HT status.

6
Assessment of potential risk factors for breast cancer in a population in Southern Brazil.
Breyer, J.Z.; Wendland, E.M.; Kops, N.L.; Caleffi, M.; Hammes, L.S.
Vol. 169 Nr. 1 Página: 125 - 131 Fecha de publicación: 01/05/2018
Resumen:
PURPOSE: The aim of this study is to assess potential risk factors for breast cancer in a population in Southern Brazil and build a multivariate logistic model using these factors for breast cancer risk prediction. METHODS: A total of 4242 women between 40 and 69 years of age without a history of breast cancer were selected at primary healthcare facilities in Porto Alegre and submitted to mammographic screening. They were evaluated for potential risk factors. RESULTS: In all, 73 participants among the 4242 women had a breast cancer diagnosis during the follow-up of the project (10 years). The multivariate analysis considering all the patients aged 40-69 years showed that older age (OR 1.08, 95% CI 1.04-1.12), higher height (OR 1.04, 95% CI 1.01-1.09), and history of previous breast biopsy (OR 2.66, 95% CI 1.38-5.13) were associated with the development of breast cancer. Conversely, the number of pregnancies (OR 0.87, 95% CI 0.78-0.98) and use of hormone replacement therapy (OR 0.39, 95% CI 0.20-0.75) were considered a protective factor. Additionally, we performed an analysis separating the participants into groups of 40-49 and 50-69 years old, since a risk factor could have a specific behavior in these age groups. No additional risk factors were identified within these age brackets, and some factors lost statistical significance. CONCLUSION: The risk prediction model indicates that the following variables should be assessed in this specific population: age, height, having had previous breast biopsies, number of pregnancies, and use of hormone replacement therapy. These findings may help to better understand the causal model of breast cancer in Southern Brazil.

7
Living with chronic pain: perceptions of breast cancer survivors.
Bao, T.; Seidman, A.; Li, Q.; Seluzicki, C.; Blinder, V.; Meghani, S.H.; Farrar, J.T.; Mao, J.J.
Vol. 169 Nr. 1 Página: 133 - 140 Fecha de publicación: 01/05/2018
Resumen:
PURPOSE: Breast cancer treatments may lead to chronic pain. For some breast cancer survivors (BCS), this experience can develop into the perception of living with chronic pain. The majority of BCS are postmenopausal and have hormone receptor-positive (HR+) breast cancer requiring aromatase inhibitors (AIs). Neither the prevalence nor risk factors associated with the perception of living with chronic pain among this population are well defined. METHODS: We conducted a cross-sectional survey among postmenopausal, HR+ BCS who previously took or were currently taking AIs. The primary outcome was patients' perception of living with chronic pain over the past 6 months. We measured pain and demographic and clinical variables. Multivariable logistic regression analysis was performed to evaluate risk factors associated with the perception of chronic pain. RESULTS: Among 1280 participants, 167 (13%) reported having the perception of living with chronic pain before their breast cancer diagnosis; 426 (34%) reported this perception after completion of non-hormonal cancer treatment. Seventy-eight percent of BCSs reported experiencing at least one type of treatment-related pain within the past 7 days, with 23% experiencing at least three types. The most common types of pain were AI-induced musculoskeletal pain (49%) and pain at the surgery or radiation site (31%). Younger age (< 56), BMI > 25, and the perception of living with chronic pain before diagnosis were risk factors associated with the perception of living with chronic pain. CONCLUSIONS: One in three postmenopausal, HR+ BCS considered themselves to be living with chronic pain. Effective interventions to reduce chronic pain are needed.

8
Adjuvant hormonal therapy for early breast cancer: an epidemiologic study of medication adherence.
Pourcelot, C.; Orillard, E.; Nallet, G.; Dirand, C.; Billion-Rey, F.; Barbier, G.; Chouk, S.; Limat, S.; Montcuquet, P.; Henriques, J.; Paget-Bailly, S.; Anota, A.; Chaigneau, L.; Nerich, V.
Vol. 169 Nr. 1 Página: 153 - 162 Fecha de publicación: 01/05/2018
Resumen:
PURPOSE: The aim of this study was to determine the prevalence of adherence to adjuvant hormonal therapy (AHT) and to identify risk factors for medication non-adherence in clinical practice in patients with early-stage hormone receptor (HR)-positive breast cancer (BC) previously treated with chemotherapy. METHODS: We carried out a cross-sectional, observational, prospective, and multicenter survey based on a structured self-report postal questionnaire (35 items investigating six areas). A sample of 474 patients was drawn from 676 patients potentially eligible. The structured and validated Morisky Medication Adherence Scale-4 items was used for measuring medication adherence. An analysis of risk factors for non-adherence to AHT was performed using a two-step approach: univariate, then multivariate analysis. RESULTS: A total of 280 patients out of the 428 analyzed patients participated in the survey, yielding a response rate of 65.4% [60.9-69.9]. The prevalence of adherence to AHT was estimated at 68.6% [63.1-74.0], corresponding to a high level of adherence. Three risk factors for non-adherence to AHT were identified: > 2 medications to treat comorbidities (p-value = 0.003), age less than 65 years (p-value = 0.008), and patient management in a university hospital setting (p-value = 0.014). CONCLUSIONS: Non-adherence is a common, complex, and multidimensional healthcare problem. This better understanding and knowledge of risk factors will allow healthcare providers (such as oncologists, general practitioners, pharmacists) to more easily identify patients at risk for non-adherence and help them provide appropriate information about AHT and its management, thus improving medication adherence in their patients.

9
Trajectories of quality of life following breast cancer diagnosis.
Goyal, N.G.; Levine, B.J.; Van Zee, K.J.; Naftalis, E.; Avis, N.E.
Vol. 169 Nr. 1 Página: 163 - 173 Fecha de publicación: 01/05/2018
Resumen:
PURPOSE: Although quality of life (QoL) improves over time for most breast cancer survivors (BCS), BCS may show different patterns of QoL. This study sought to identify distinct QoL trajectories among BCS and to examine characteristics associated with trajectory group membership. METHODS: BCS ($N = 653$) completed baseline assessments within 8 months of diagnosis. QoL was assessed by the Functional Assessment of Cancer Therapy-Breast (FACT-B) at baseline and 6, 12, and 18 months later. Finite mixture modeling was used to determine QoL trajectories of the trial outcome index (TOI; a composite of physical well-being, functional well-being, and breast cancer-specific subscales) and emotional and social/family well-being subscales. Chi-square tests and F tests were used to examine group differences in demographic, cancer-related, and psychosocial variables. RESULTS: Unique trajectories were identified for all three subscales. Within each subscale, the majority of BCS had consistently medium or high QoL. The TOI analysis revealed only stable or improving groups, but the emotional and social/family subscales had groups that were stable, improved, or declined. Across all subscales, women in "consistently high" groups had the most favorable psychosocial characteristics. For the TOI and emotional subscales, psychosocial variables also differed significantly between women who started similarly but had differing trajectories. CONCLUSIONS: The majority of BCS report good QoL as they transition from treatment to survivorship. However, some women have persistently low QoL in each domain and some experience declines in emotional and/or social/family well-being. Psychosocial variables are consistently associated with improving and/or declining trajectories of physical/functional and emotional well-being.

10
Patient-reported outcomes of catheter-based accelerated partial breast brachytherapy and whole breast irradiation, a single institution experience.
Jethwa, K.R.; Kahila, M.M.; Mara, K.C.; Harmsen, W.S.; Routman, D.M.; Pumper, G.M.; Corbin, K.S.; Sloan, J.A.; Ruddy, K.J.; Hieken, T.J.; Park, S.S.; Mutter, R.W.
Vol. 169 Nr. 1 Página: 189 - 196 Fecha de publicación: 01/05/2018
Resumen:
PURPOSE: Accelerated partial breast irradiation (APBI) and whole breast irradiation (WBI) are treatment options for early-stage breast cancer. The purpose of this study was to compare patient-reported-outcomes (PRO) between patients receiving multi-channel intra-cavitary brachytherapy APBI or WBI. METHODS: Between 2012 and 2015, 131 patients with ductal carcinoma in situ (DCIS) or early stage invasive breast cancer were treated with adjuvant APBI (64) or WBI (67) and participated in a PRO questionnaire. The linear analog scale assessment (LASA), harvard breast cosmesis scale (HBCS), PRO-common terminology criteria for adverse events- PRO (PRO-CTCAE), and breast cancer treatment outcome scale (BCTOS) were used to assess quality of life (QoL), pain, fatigue, aesthetic and functional status, and breast cosmesis. Comparisons of PROs were performed using t-tests, Wilcoxon rank-sum, Chi square, Fisher exact test, and regression methods. RESULTS: Median follow-up from completion of radiotherapy and questionnaire completion was 13.3 months. There was no significant difference in QoL, pain, or fatigue severity, as assessed by the LASA, between treatment groups ($p > 0.05$). No factors were found to be predictive of overall QoL on regression analysis. BCTOS health-related QoL scores were similar between treatment groups ($p = 0.52$).The majority of APBI and WBI patients reported excellent/good breast cosmesis, 88.5% versus 93.7% ($p = 0.37$). Skin color change ($p = 0.011$) and breast elevation ($p = 0.01$) relative to baseline were more common in the group receiving WBI. CONCLUSIONS: APBI and WBI were both associated with favorable patient-reported outcomes in early follow-up. APBI resulted in a lesser degree of patient-reported skin color change and breast elevation relative to baseline.