

**PERÚ****Sector
Salud****Instituto Nacional de Enfermedades
Neoplásicas**

DECENIO DE LA IGUALDAD DE OPORTUNIDADES PARA MUJERES Y HOMBRES
"AÑO DEL BICENTENARIO DEL PERÚ: 200 AÑOS DE INDEPENDENCIA"

MAMAS Y TEJIDOS BLANDOS

➤ **Adaptation of international coronavirus disease 2019 and breast cancer guidelines to local context**

INVESTIGADORES: Guillermo Arturo Valencia, Silvia Neciosup, Henry L Gómez, Maria Del Pilar Benites, Silvia Falcón, David Moron, Karin Veliz, Mike Maldonado, Rodrigo Auqui.

REVISTA: World J Clin Oncol 2021 Jan 24;12(1):31-42. doi: 10.5306/wjco.v12.i1.31.

ABSTRACTO: Background: The coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (a novel coronavirus), which was first identified amid an outbreak of respiratory illness cases in Wuhan, China and declared a global health emergency, is currently considered an additional challenge in the management of patients with breast cancer (BC). Cancer patients are more vulnerable to becoming infected with severe acute respiratory syndrome coronavirus 2 and are more likely to suffer additional complications that can increase mortality. Identifying those BC patients who require more urgent therapy than others in the current situation is essential. These recommendations are based on and have been adapted from those similarly published by international scientific societies for BC management. They are divided mainly by clinical stage (early, advanced), subtype [luminal, human epidermal growth factor receptor 2 (HER2), triple-negative], or type of medical treatment and setting (neoadjuvant, adjuvant, metastatic). Recommendations for HER2 and triple-negative subtypes are similar, whereas in luminal subtype there are various options of management. The objective is to adapt guidelines to local context through relevant decision-makers, avoiding duplication of efforts and optimizing use of resources. We hope that these recommendations will help medical oncologists provide the best quality care to BC patients during the COVID-19 pandemic with information tailored to our healthcare system. Aim: To establish and adapt recommendations from those published by international scientific societies for BC management. Methods: The Peruvian Society of Medical Oncology developed a consensus and propose here a manuscript with recommendations for oncological medical treatment of BC during the COVID-19 pandemic. The Peruvian Society of Medical Oncology invited a panel of experts and opinion leaders on BC working in major health care systems around Peru. Panel experts selected three international clinical practice guidelines (National Comprehensive Cancer Network, European Society for Medical Oncology, Spanish Foundation Research Group in Breast Cancer), considering that these are more representative in COVID-19 management. Also, the panel agreed to include at least one European and American clinical practice guideline. Results: Recommendations about BC management during the COVID-19 pandemic were divided mainly by clinical stage (early, advanced), subtype (luminal, HER2, triple-negative), or type of medical treatment and setting (neoadjuvant, adjuvant, metastatic). Recommendations for HER2 and triple-negative subtypes were similar between clinical practice guidelines, whereas in luminal subtype there were various options of management. One hundred twelve recommendations were reviewed, adapted, and voted. A consensus was made in order to provide best decisions of management, avoid duplication of efforts, and optimize medical resources, considering health care system reality. These recommendations are not intended to replace clinical judgment. Conclusion: Most of recommendations are



similar, mainly in high-risk subtypes (HER2, triple- negative). Certain societies adapt them to deal with different situations involving the best decision in the management of BC patients.

➤ **PUM1 and RNase P genes as potential cell-free DNA markers in breast cancer**

INVESTIGADORES: Alexis Murillo Carrasco, Oscar Acosta, Jaime Ponce, José Cotrina, Alfredo Aguilar, Jhajaira Araujo, Pamela Rebaza, Joseph A Pinto, Ricardo Fujita, José Buleje.

REVISTA: J Clin Lab Anal 2021 Feb 1;e23720. doi: 10.1002/jcla.23720.

ABSTRACTO: Background: Cell-free DNA (cfDNA) is used in clinical research to identify biomarkers for diagnosis of and follow-up on cancer. Here, we propose a fast and innovative approach using traditional housekeeping genes as cfDNA targets in a copy number analysis. We focus on the application of highly sensitive technology such as digital PCR (dPCR) to differentiate breast cancer (BC) patients and controls by quantifying regions of PUM1 and RPPH1 (RNase P) in plasma samples. Methods: We conducted a case- control study with 82 BC patients and 82 healthy women. cfDNA was isolated from plasma using magneticbeads and quantified by spectrophotometry to estimate total cfDNA. Then, both PUM1 and RPPH1 genes were specifically quantified by dPCR. Data analysis was calibrated using a reference genomic DNA in different concentrations. Results: We found RNase P and PUM1 values were correlated in the patient group (intraclass correlation coefficient [ICC] = 0.842), but they did not have any correlation in healthy women (ICC = 0.519). In dPCR quantification, PUM1 showed the capacity to distinguish early-stage patients and controls with good specificity (98.67%) and sensitivity (100%). Conversely, RNase P had lower cfDNA levels in triple-negative BC patients than luminal subtypes ($p < 0.025$ for both), confirming their utility for patient classification. Conclusion: We propose the PUM1 gene as a cfDNA marker for early diagnosis of BC and RNase P as a cfDNA marker related to hormonal status and subtype classification in BC. Further studies with larger sample sizes are warranted.

➤ **A novel AAGAB mutation in a Peruvian family with punctate palmoplantar keratoderma**

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REVISTA: Acta Dermatovenerol Alp Pannonica Adriat 2021 Mar;30(1):47-48.

ABSTRACTO: Buschke-Fischer-Brauer (BFB) disease is a rare keratoderma characterized by multiple hyperkeratotic lesions on the palms and soles, with an autosomal dominant pattern. In several countries, some genetic alterations have been associated with this clinical entity. A 68-year-old Peruvian woman presenting with hyperkeratotic lesions on both her palms and soles was diagnosed with BFB keratoderma. After sequencing of the genes that had previously been related to this disease, a mutation (c.249C>G) that was predicted to generate a termination codon (Tyr83*) was found in the alpha and gamma adaptin binding protein P34 gene (AAGAB). After treatment with 30% urea plus 10% salicylic acid, the patient experienced an improvement in her condition. Here we report a novel mutation in the AAGAB gene of a patient diagnosed with BFB keratoderma and a treatment that improved her symptoms.

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➤ **Evaluation of diagnostic ultrasound use in a breast cancer detection strategy in Northern Peru**

INVESTIGADORES: Segen Aklilu, Carolyn Bain, Pooja Bansil, Silvia de Sanjose, Jorge A Dunstan, Vanesa Castillo, Vivien Tsu, Ines Contreras, Ronald Balassanian, Tara K Hayes Constant, John R Scheel.

REVISTA: PLoS One 2021 Jun 11;16(6):e0252902. doi: 10.1371/journal.pone.0252902. eCollection2021.

ABSTRACTO: To evaluate the diagnostic impact of point-of-care breast ultrasound by trained primary care physicians (PCPs) as part of a breast cancer detection program using clinical breast exam in an underserved region of Peru. Medical records and breast ultrasound images of symptomatic women presenting to the Breast Cancer Detection Model (BCDM) in Trujillo, Peru were collected from 2017-2018. Performance was measured against final outcomes derived from regional cancer center medical records, fine needle aspiration results, patient follow-up (sensitivity, specificity, positive, and negative predictive values), and by percent agreement with the retrospective, blinded interpretation of images by a fellowship-trained breast radiologist, and a Peruvian breast surgeon. The diagnostic impact of ultrasound, compared to clinical breast exam (CBE), was calculated for actual practice and for potential impact of two alternative reporting systems. Of the 171 women presenting for breast ultrasound, 23 had breast cancer (13.5%). Breast ultrasound used as a triage test (current practice) detected all cancer cases (including four cancers missed on confirmatory CBE). PCPs showed strong agreement with radiologist and surgeon readings regarding the final management of masses (85.4% and 80.4%, respectively). While the triage system yielded a similar number of biopsies as CBE alone, using the condensed and full BI-RADS systems would have reduced biopsies by 60% while identifying 87% of cancers immediately and deferring 13% to six-month follow-up. Point-of-care ultrasound performed by trained PCPs improves diagnostic accuracy for managing symptomatic women over CBE alone and enhances access. Greater use of BI-RADS to guide management would reduce the diagnostic burden substantially.

➤ **The current situation regarding the availability and accessibility of anticancer drugs for breast cancer in the Peruvian public health systems**

INVESTIGADORES: Guillermo Valencia-Mesías, Patricia Rioja-Viera, Zaida Morante-Cruz, Yura Toledo-Morote, Silvia Neciosup-Delgado, Henry Gómez-Moreno.

REVISTA: Ecancermedicalscience 2021 Apr 27;15:1224. doi: 10.3332/ecancer.2021.1224. eCollection 2021.

ABSTRACTO: The availability of effective, accessible, safe and high-quality anticancer drugs for the medical treatment of cancer is fundamental in ensuring optimal healthcare in the public health system in Peru. The main objective is to assess the current situation regarding anticancer drugs (termed 'high-cost') for breast cancer, as well as an analysis of the possible factors which negatively impact access to the Peruvian public health systems. There are similarities in the availability of anticancer drugs, since most treatments are covered by the Peruvian Ministry of Health. EsSalud offers an extra monoclonal antibody (pertuzumab) in the metastatic treatment stage. Meanwhile, the National Institute of Neoplastic Diseases (INEN), mainly for metastatic disease, has relied on more tested treatments over the last year. An agreement has been reached with the armed forces, which will enable patients to receive oncology care at the INEN and, thereby, benefit from the use of high-cost drugs.



➤ **Biological characteristics of a sub-population of cancer stem cells from two triple-negative breast tumour cell lines**

INVESTIGADORES: Javier Enciso-Benavides, Luis Alfaro, Carlos Castañeda-Altamirano, Nancy Rojas, José González-Cabeza, Nathaly Enciso, Fernando Riesco, Miluska Castillo, Javier Enciso.

REVISTA: Heliyon 2021 Jun 10;7(6):e07273. doi: 10.1016/j.heliyon.2021.e07273. eCollection 2021 Jun.

ABSTRACTO: Triple-negative breast tumours (TNBTs) make up 15-20% of all breast tumours. There is no treatment for them, and the role that cancer stem cells (CSCs) have in carcinogenesis is still unclear, so finding markers and therapeutic targets in CSC exosomes requires these cells to exist as a homogeneous cell population. The objective of this work was to determine differences in ultrastructural morphology, proliferative capacity, and mouse-xenotransplantation characteristics of the MDA-MB-231 and MDA-MB-436 TNBT cell lines with the CD44 high /CD24 low phenotype in order to study their exosomes. The results show that the CD44 high /CD24 low MDA-MB-231 cells had a population doubling time of 41.56 h, compared to 44.79 h in the MDA-MB-436 cell line. After magnetic immunoseparation, 18.75% and 14.56% of the stem cell population of the MDA-MB-231 and MDA-MB-436 cell lines, respectively, were of the CD44 high /CD24 low phenotype, which were expanded to reach purities of 80.4% and 87.6%. The same expanded lineage in both cell lines was shown to possess the pluripotency markers Nanog and Oct4. Under a scanning electron microscope, the CD44 high /CD24 low lineage of the MDA-MB-231 cell line formed groups of more interconnected cells than this lineage of the MDA-MB-436 line. A total of 16% of the mice inoculated with the CD44 high /CD24 low lineage of either cell line presented tumours of the breast, lung, and submandibular ganglia, in whose tissues variable numbers of inoculated cells were found 30 days post-inoculation. By magnetic immunoselection, it was possible to isolate in similar quantities and characterize, expand, and xenotransplant the CD44 high /CD24 low lineage of the MDA-MB-231 and MDA-MB-436 cell lines. The former cell line has greater proliferative capacity, the two lines differ under scanning electron microscopy in how they intercommunicate, and both cell lines induce new tumours in mice and persist at least 30 days post-inoculation in the transplanted animal so their exosomes would also be different.

➤ **Recomendaciones para el tratamiento médico oncológico del cáncer de mama ante la pandemia de COVID-19**

INVESTIGADORES: Guillermo Valencia, María del Pilar Benites, Silvia Falcón, Karin Veliz, Mike Maldonado, David Morón, Rodrigo Auqui, Silvia Neciosup, Henry Gómez.

REVISTA: Carcinoma 2020; 10(1): 28-39.

ABSTRACTO: La pandemia de COVID-19 es considerada actualmente un desafío adicional en el manejo de los pacientes con cáncer de mama (CM). Los pacientes con CM son más vulnerables a infectarse con SARS-CoV-2, y tienen una mayor probabilidad de sufrir complicaciones adicionales que pueden aumentar su mortalidad. Identificar a los pacientes con CM que requieren una terapia más urgente que otros (incluso hasta después de la pandemia) en la coyuntura actual es fundamental; por lo tanto, la Sociedad Peruana de Oncología Médica (SPOM) ha emitido recomendaciones para su



tratamiento, las cuales se basan y han sido adaptadas a partir de las recomendaciones de sociedades científicas internacionales. SPOM invitó a líderes de opinión y expertos en CM que laboran en las principales instituciones de salud pública y privada en Perú, y se realizó un consenso. Estas recomendaciones se dividen principalmente por estadio clínico (temprano y avanzado), subtipo (luminal, HER2 y triple negativo) o tipo de tratamiento médico (escenario neoadyuvante, adyuvante y metastásico). Las recomendaciones para los subtipos HER2 y triple negativo son similares, mientras que en el subtipo luminal existen varias opciones de manejo. El objetivo es adaptar las directrices en el contexto local a través de toma de decisiones relevantes, evitando duplicación de esfuerzos y optimizando el uso de recursos. Estas recomendaciones permiten a los médicos oncólogos a brindar una atención de calidad a los pacientes con CM durante la pandemia de COVID-19 con información adaptada a nuestra realidad nacional.

➤ **Cirugía mamaria oncoplástica extrema**

INVESTIGADORES: Fiorella Oré, María Ramos, Milagros Amorín, José Cotrina.

REVISTA: Carcinomas 2019; 9(1): 41-44.

ABSTRACTO: La cirugía oncoplástica extrema (COE) está emergiendo como un nuevo concepto en cirugía de cáncer de mama, permitiendo realizar cirugía conservadora de mama (CCM) en pacientes seleccionados con tumores multicéntricos, tumores mayores a 5cm o lesiones extensas a pesar de neoadyuvancia y que tendrían indicación de mastectomía. Se presenta el caso de una mujer de 36 años con un tumor en mama derecha asociado a microcalcificaciones extensas. Recibió tratamiento neoadyuvante con quimioterapia, y posteriormente se realizó una cuadrantectomía guiada por aguja Hawkins con patrón vertical, biopsia de ganglio centinela, y simetrización contralateral simultánea con patrón de doble rama. El resultado oncológico (bordes libres) y estético fue exitoso.

➤ **Metástasis ovárica de cáncer de mama**

INVESTIGADORES: María Ramos, José Cotrina, Marco Velarde, Martín Falla, Fiorella Oré, Milagros Amorín, Renier Cruz, Henry Guerra.

REVISTA: Carcinomas 2019; 9(2): 45-50.

ABSTRACTO: Las metástasis más frecuentes por cáncer de mama se encuentran en el hígado, pulmones y huesos; sin embargo, la afectación ovárica no es tan rara como se podría pensar, llegando a reportarse en el 30% de los casos en algunos estudios. Frecuentemente el diagnóstico es tardío, por falta de sospecha inicial. Se presenta el caso de una mujer de mediana edad que debuta con un cáncer de mama derecha, se le brindó tratamiento quirúrgico (mastectomía radical), y tratamiento adyuvante con quimioterapia y radioterapia. Posteriormente, se realizó ablación quirúrgica con ooforectomía bilateral, detectándose incidentalmente metástasis ovárica asintomática. Actualmente, la paciente está siendo tratada con anastrozol y continúa en controles.