eBreast

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Práctica Cáncer de Mama

MANUAL PRÁCTICO PARA LA CONSULTA DE PACIENTES CON CÁNCER DE MAMA

NOVARTIS

ES2208313850

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Avales

PARA INFORMACIÓN ADICIONAL, CONSULTAR EL RESTO DE LOS CAPÍTULOS

ISBN: 978-84-09-22045-8

PRÓLOGO

eBreast nace como signo de los tiempos.

No es un libro.

No es una app.

Es la respuesta a las nuevas formas de aprender, enseñar y estudiar.

Signo de los tiempos por la importancia y el impacto que tiene el cáncer de mama en nuestra sociedad y en nuestro sistema sanitario.

Signo de los tiempos por la incesante llegada de nuevos profesionales que tienen la gran responsabilidad de cuidar a nuestras pacientes afectas de cáncer de mama y con la necesidad de adquirir un conocimiento riguroso, actualizado y de acceso inmediato, a veces en la propia consulta, para poder ofrecer las mejores opciones que la evidencia científica nos proporciona.

Signo de los tiempos por la forma de enfrentarse a la información. La aparición y expansión de nuevas TIC (Tecnologías de la información y comunicación), algunas de ellas rápidamente absorbidas por las nuevas generaciones, hace preciso adaptarse a ellas.

Signo de los tiempos por el enorme volumen de información que se genera a diario y que hace precisa la intervención de revisores autorizados en cada materia, sobre todo para los clínicos. El fondo de conocimiento médico es inabarcable. Y el conocimiento y el progreso oncológicos son, actualmente, de los más importantes en la medicina moderna: por volumen de publicaciones, recursos que se destinan, impacto social, consecuencias de la enfermedad…

eBreast está dirigido a todos aquellos profesionales que atienden una consulta médica de cáncer de mama, sobre todo a los que se inician en la patología, a los que atienden a estas pacientes de forma más esporádica o simplemente a los que desean mantenerse actualizados. eBreast proporciona una consulta rápida, sencilla y, sobre todo, muy visual e interactiva. Y con este proyecto nos comprometemos a revisar periódicamente los contenidos, actualizando los datos tras los principales acontecimientos científicos del año.

Los coordinadores quisiéramos agradecer el inmenso esfuerzo realizado por todos los autores, así como el apoyo proporcionado por Novartis, y a las sociedades GEICAM, SEOM, SOLTI y a la Universidad CEU Cardenal Herrera por su aval.

No queremos dejar de olvidar el apoyo de nuestras familias y, sobre todo, a LOS/LAS PACIENTES afectos de cáncer de mama, que son el objeto de todos nuestros esfuerzos, estudios y desvelos profesionales y por tanto, los beneficiarios finales de este proyecto, que pretende ser novedoso.

Santiago Olmos Antón **Eduardo Martínez de Dueñas**

ABREVIATURAS

A	Antraciclina
AC	Adriamicina/doxorrubina, ciclofosfamida
ACT	Antraciclina-ciclofosfamida y taxano concurrente
AC-T	Antraciclina-ciclofosfamida y taxano secuencial
AC-D	Adriamicina, ciclofosfamida, docetaxel
AL	Adriamicina Liposomal
ALND	*Axillary lymph node dissection*
AMH	Agente modulador del hueso
ANA	Anastrozol
AO	Ablación ovárica
AP	Adriamicina,paclitaxel
APBI	Radioterapia parcial acelerada
AP-CMF-Q(x)	Adriamicina y paclitaxel-quimioterapia de ciclofosfamida, metotrexato y 5-FU
AP-CMF	Adriamicina y paclitaxel, ciclofosfamida, metotrexato y 5-FU
ASCO	*Sociedad Americana de Clínica Oncología*
AxRT:	*Axillary radiotherapy*
B	Bevacizumab
BAG	Biopsia con aguja gruesa
BAV	Biopsia asistida por vacío
BC	Beneficio clínico
BCS	Supervivencia específica por cáncer de mama
BOADICEA	*Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm*
BSGC	Biopsia selectiva del ganglio centinela
CAF/FAC	Ciclofosfamida, adriamicina y 5-FU
CAFM	Ciclofosfamida, adriamicina, 5-FU y metroxetato
C	Cirugía/Carboplatino
CAP	Capecitabina
CC	Cirugía conservadora
CDDP	Cisplatino
CDI	Carcinoma ductal invasivo

CDIS	Carcinoma ductal *in situ*
CDK	Cinasas dependientes de ciclinas
CEA	Antígeno carcinoembriónico
CEF/FEC	Ciclofosfamida, epirrubicina, 5-FU
CLI	Carcinoma lobulillar infiltrante
CM	Cáncer de mama
CMAJ	*Canadian Medical Association Journal*
CMF	Ciclofosfamida, metotrexato y 5-FU
CMI	Cáncer de mama inflamatorio
CMLA	Cáncer de mama localmente avanzado
CMM	Cáncer de mama metastásico
CMTN	Cáncer de mama triple negativo
cN+	Ganglios linfáticos positivos clínicamente
C-A-CMF	Cirugía-antraciclina-ciclofosfamida, metotrexato y 5-FU
C-AP-CMF	Cirugía-adriamicina, paclitaxel-ciclofosfamida, metotrexato y 5-FU
D	Docetaxel
ddAC	Dosis densas adriamicina y ciclofosfamida
DMO	Densidad mineral ósea
DX	Doxorrubicina
EBCTCG	*Early Breast Cancer Trialists' Collaborative Group*
EC	Epirrubicina, ciclofosfamida
ECG	Electrocardiograma
ECO	Ecografía
ED	Epirrubicina, docetaxel
ESA	Agente estimulador de la eritropoyesis
ESMO	European Society for Medical Oncology
EXE	Exemestano
F	Fulvestrant
FEVI	Fracción de eyección ventricular izquierda
FN	Fiebre neutropénica
GC	Ganglio centinela
GnRH	Hormona liberadora de gonadotropina

G-CSF	Factor estimulante de colonias de granulocitos
TR	Trastuzumab
HD	Altas dosis
HER/EGFR	Receptor de factor de crecimiento epidérmico humano
HNA	Hormonoterapia neoadyuvante
HR	*Hazard ratio*
HT	Hormonoterapia
IA	Inhibidores aromatasa
IAE	Inhibidor no esteroideo de la aromatasa
IANE	Inhibidor de la no esteroideo de la aromatasa
IC	Intervalo de confianza
ICT	Células tumorales aisladas
IHQ	Inmunohistoquímico
ILE	Intervalo libre de enfermedad
IPM	Irradiación parcial de la mama
ISH	Hibridación *in situ*
L	Lapatinib
LA	Linfadenectomía axilar
LET	Letrozol
LHRH	Hormona liberadora de la hormona luteinizante
LR-SLP	Supervivencia libre de progresión locorregional
MMSE	*Mini-Mental State Examination*
MNA	*Mini nutritional assessment*
MRM	Mastectomía radical modificada
MT	Marcadores tumorales
N.A	No aportado
NAB-P	nab-paclitaxel (paclitaxel unido a albúmina)
NCCN	*National Comprehensive Cancer Network*
NCI	*National Cancer Institute*
NCI-CTCAE	*National Cancer Institute Common Terminology Criteria for Adverse Events*
N.S	No significativo
NSABP	*National Surgical Adjuvant Breast and Bowel Project*

OCCR	*Ovarian Cancer Cluster Region*
OR	*Odds Ratio*
ORR	*Objective response rate*
OSNA	*One step nucleic acid amplification*
P	Paclitaxel
PA	Palbociclib
PAAF	Punción aspiración con aguja fina
PE	Progresión de la enfermedad/pertuzumab
PEPI	*Preoperative Endocrine Prognostic Index*
PER	Pertuzumab
PET	Tomografía por emisión de positrones
PF	Preservación de la fertilidad
Post-Op	Postoperatorio
PP	Profilaxis primaria
pRC	Respuesta patológica completa
Pre-Op	Preoperatorio
pRP	Respuesta parcial patológica
pRPmic	Respuesta parcial patológica microscópica
PS	Profilaxis secundaria
QoL	Calidad de vida
QT	Quimioterapia
RANKL	Ligando del receptor activador del factor nuclear k-B
RC	Respuesta completa
RCB	*Residual Cancer Burden* (enfermedad residual posquimioterapia)
RE	Receptor de estrógeno
RFS	Supervivencia libre de recaída
RH	Receptor hormonal
RMN	Resonancia magnética nuclear
ROI	Rastreo óseo isotópico/ gamma o escintigrafía ósea
RP	Receptor de progesterona/Respuesta parcial
RR	Riesgo de recaída
RS	Recurrence score

RT	Radioterapia
Rx	Radiografía
SBRT	Radioterapia estereotáctica de cuerpo
SC	Subcutáneo
SERD	Inhibidor selectivo del RE
SERMS	Modulador selectivo del receptor estrogénico
SG	Supervivencia global
SLE	Supervivencia libre de enfermedad
SLP	Supervivencia libre de progresión
SLR	Supervivencia libre de recaída
SNP	*Single nucleotide polymorphism*
SPPB	Batería corta de rendimiento físico
ST	Tratamiento sistémico
T	Taxano
TA	Tratamiento adyuvante
TAC	Tomografía axial computarizada o Docetaxel, adriamicina, ciclofosfamida
TAM	Tamoxifeno
TBCRC	*Translational Breast Cancer Research Consortium*
TC	Docetaxel y ciclofosfamida
TCH	Docetaxel, carboplatino, trastuzumab
T-DM1	Trastuzumab emtansina
TE	Terapia endocrina
TIL	*Tumor Infiltrating Lymphocites*
THP	Tiempo hasta progresión
TMA	Transplante de células madre autólogo
TN	Triple negativo
TNA	Tratamiento neoadyuvante
TR	Trastuzumab
UCGC	Unidad de consejo genético en cáncer
UI	Unidades Internacionales
V	Vinorelbina

CAPÍTULO 2. MANEJO LOCOREGIONAL

A. MANEJO DE LA AXILA

¿Cómo se valoran los ganglios axilares?

¿Cómo se realiza el estudio histopatológico del Ganglio Centinela?

¿Cómo se maneja la axila clínicamente negativa?

¿Cómo se maneja la axila clínicamente positiva?

¿Cómo manejar la axila si la paciente va a recibir quimioterapia neoadyuvante?

VER RESUMEN
2. Manejo locoregional
a) Manejo de la axila

¿Cómo se valoran los ganglios axilares?

ESTUDIO DE LOS GANGLIOS AXILARES

La afectación de los ganglios axilares es el factor pronóstico clásico más importante.

Linfadenectomía axilar (LA):

- Consiste en la extirpación de los niveles axilares I y II.
- Presenta una morbilidad y un deterioro de la calidad de vida importantes (linfedema y dolor posmastectomía, linfangitis…).
- Establecida como el estándar en el siglo XIX, lo sigue siendo durante la mayor parte del XX por su valor pronóstico y terapéutico, hasta que un ensayo clínico aleatorizado, el NSABP B-04 (51) descarta su valor terapéutico.
- La necesidad de mantener la información pronóstica y disminuir la morbilidad lleva al desarrollo de la biopsia selectiva del ganglio centinela.

Biopsia selectiva ganglio centinela (BSGC):

- **Actualmente es la aproximación estándar** ante los resultados del ensayo NSABP B-32 (52), que puso de manifiesto que la probabilidad de predecir el estatus del resto de la axila es superior al 95 % y la tasa de falsos negativos del 5-10 %, pero la recaída axilar menor del 1 % (entre 0,4 y 0,8 %), sin afectación en la supervivencia.
- Consiste en la inyección periareolar/peritumoral de un contraste (radioactivo, colorante o ambos) y la detección en el quirófano del primer o primeros ganglios del drenaje linfático, su extirpación y estudio para ver si están afectados.
- Presenta mucha menos morbilidad que la linfadenectomía axilar (15 al 20 % de linfedema con linfadenectomía, frente a menos de un 3 % con BSGC).

¿Cómo se realiza el estudio histopatológico del Ganglio Centinela?

Estudio histopatológico del ganglio centinela

- Debe ser intraoperatorio siempre que sea posible para evitar dos intervenciones.
- El estudio se puede realizar por:
  - Estudio de cortes por congelación. No se recomienda el uso de IHQ o RT-PCR para identificar micrometástasis ocultas, ya que se desconoce su impacto en el pronóstico y tratamiento.
  - OSNA (*One step nucleic acid amplification*).
    - Estudia el ganglio en su totalidad.
    - Solo se puede realizar en tumores que expresan CK19.

Tabla 11. Relación TNM y OSNA. ***Adaptada de Bernet L. et al. (53).***

RESULTADOS	Método clásico	OSNA (n.º copias)
Macrometástasis	> 2 mm	> 5000
Micrometástasis	≤ 2 mm	De 250 a 5000
Células tumorales aisladas	< 0,2 mm	

¿Cómo se maneja la axila clínicamente negativa?

MANEJO DE LA AXILA CLÍNICAMENTE NEGATIVA

Se considera la axila clínicamente negativa o N0 clínico cuando la exploración y la ecografía axilar son negativas y tiene indicación de **realizar BSGC**.

BSGC (-):

Alta probabilidad de axila negativa. **No se realiza linfadenectomía**.

BSGC (+):

Micrometástasis:

Estudios actuales como el ensayo IBCSG 23-01 (54) indican que **no es necesaria la realización de una linfadenectomía** axilar.

Macrometástasis:

A.- Metástasis no masivas en uno o dos ganglios (+):

Más discutido es si puede evitarse la LA, ya que el estudio ACOSOG ZOO11 (55), de no inferioridad, no detectó diferencias en recaída local ni supervivencia frente a LA. Por otra parte, hay que tener en cuenta que en este ensayo todas las pacientes debían cumplir lo siguiente:

- Tumores menores de 5 cm
- Cirugía conservadora (tumorectomía)
- Máximo 1 o 2 ganglios centinelas positivos sin extensión extracapsular
- Haber recibido tratamiento sistémico y radioterapia
- No tener ganglios palpables

Tabla 12. Estudio ACOSOG Z0011: recaídas, SLE y SG. ***Adaptada de Giuliano A.E. et al. (55).***

ACOSOG Z0011	BSGC sola	BSGC + LA	p valor
Recaída locorregional 5 años	1,6 %	3,1 %	0,11
SG 5 años	92,5 %	91,8 %	0,25
SLE 5 años	83,9 %	82,2 %	0,14

SG: supervivencia global; SLE: supervivencia libre de enfermedad; BSGC: biopsia selectiva ganglio centinela; LA: linfadenectomía axilar.

Por otra parte, el estudio AMAROS (56) de no inferioridad, que en pacientes con BSGC(+) compara la LA con la radioterapia axilar, no encuentra diferencias en el control axilar, que es excelente: la RECAÍDA axilar a los 5 años fue del 0,43 % (IC 95 % 0,00-0,92) en el grupo de linfadenectomía axilar (4/744 pacientes) y del 1,19 % (0,31-2,08) (7/681 pacientes) en el grupo de radioterapia axilar (el margen de no inferioridad era de 2).

No hubo diferencias significativas en SLE y supervivencia global entre los grupos de tratamiento.

Por todo esto, algunos autores recomiendan que en aquellas **pacientes que cumplan los criterios del ACOSOGZ0011, si tienen uno o dos ganglios centinelas (+), se pueda evitar la LA**, y en las que no cumplen esos criterios se realice una linfadenectomía.

B.- Afectación masiva, ≥3 GANGLIOS (+), o existe rotura capsular:

Indicación de LA.

¿Cómo se maneja la axila clínicamente positiva?

MANEJO DE LA AXILA CLÍNICAMENTE POSITIVA

Si existen ganglios palpables y/o confirmación de anatomía patológica (PAAF o biopsia), si la paciente no es candidata a quimioterapia neoadyuvante, **es indicación de linfadenectomía**.

¿Cómo manejar la axila si la paciente va a recibir quimioterapia neoadyuvante?

MANEJO DE LA AXILA Y NEOADYUVANCIA

- En las pacientes que van a recibir quimioterapia neoadyuvante, a aquellas con ***cáncer de mama operable (T2-3, N0-1)*** se les puede realizar **BSGC, ya sea pre o posquimioterapia**, porque la mayoría de los datos provienen de este grupo de pacientes (la seguridad y exactitud del resultado son cuestionables en tumores T4 o N2, por lo que no debe utilizarse).
- Por otra parte, la quimioterapia neoadyuvante infraestadía la axila positiva "CON TASAS DE RCp AXILAR entre un 40 y un 68% en tumores HER2 dependiente de RH (mayor en RH negativos) y prácticamente UN 35% de los casos de los triple negativos (57).
- La utilización de la BSGC pre o posquimioterapia es un tema controvertido.

AXILA NEGATIVA:

1.- BSGC prequimioterapia neoadyuvante:

Útil en axila clínicamente negativa, pero tiene los siguientes **inconvenientes**:

- Puede extirpar el único ganglio positivo, con lo que interfiere en la valoración de la quimiosensibilidad.
- Requiere dos procedimientos quirúrgicos.

2.- BSGC posquimioterapia neoadyuvante:

En la axila negativa existen múltiples estudios, y un metaanálisis de 24 ensayos evidenció que es una técnica válida para estas pacientes, con **tasas de detección del 90 % y de falsos negativos del 8 %**. Para algunos autores debería considerarse el estándar (58, 59).

VER RESUMEN
2. Manejo locoregional
a) Manejo de la axila
Manejo de la Axila clínicamente negativa

AXILA POSITIVA:

VER RESUMEN
2. Manejo locoregional
a) Manejo de la axila
Manejo de la Axila clínicamente positiva

1.- Linfadenectomía:

La actuación habitual hasta la fecha.

2.- BSGC posquimioterapia neoadyuvante:

En la axila positiva documentada, la realización de BSGC podría permitir evitar la LA (60) en aquellas pacientes con RC en axila, sobre todo en HER2 positivo y triple negativo.

Tres estudios prospectivos aleatorizados: ACOSOC Z1071 (61), SENTINA (62) y SN FNAC (63) objetivaron tasas de detección ligeramente menores que en la pre-QT (entre el 80 y el 93 % vs. el 95 %), mientras que la tasa de falsos (-) fue de entre el 9,6 y el 13 %, pero afectadas predominantemente por el número de ganglios centinelas extirpados.

Tabla 13. Resultados de los estudios ACOSOG, SN FNAC y SENTINA. ***Creada por el autor.***

Pacientes con axila (+) y realización de BSGC tras QT neoadyuvante

	ACOSOG Z1071 (61)	SENTINA (62)	SN FNAC (63)
N.º Pacientes	756	592	153
Falsos (-) con 1 GC	31,5 %	24,3 %	18,2 %
Falsos (-) con ≥2 GC	12,6 %	18,5 %*	4,9 %
Falsos (-) con 2 trazadores	10,8 %	8,6 %	5,2 %
Falsos (-) con 1 trazador	20,3 %	16 %	16 %

*GC: ganglio centinela. *Solo dos ganglios centinela*

El estudio ACOSOG Z1071 mostró que la tasa de falsos negativos (TFN) de la BSGC tras la quimioterapia neoadyuvante y al menos dos ganglios centinela identificados era del 12,6 %, y aunque estos datos sugieren que no parece segura la BSGC tras la neoadyuvancia, se identifican factores importantes que influyen en la TFN, siendo significativamente más baja cuando se utilizan dos marcadores y con mayor número de GC identificados.

Ante estas tasas de falsos negativos tan altas, **no se considera un procedimento estándar**, aunque algunos autores encuentran una reducción de esta tasa hasta 2 % si se realizan las siguientes recomendaciones (18):

- Marcar con clip los ganglios (+) confirmados con AP antes de la quimioterapia.
- Utilizar dos agentes de marcado (radioisótopo y colorante).
- Identificar y extirpar dos o más ganglios más los marcados con clip.
- Considerar realizar en este caso IHQ y, si todo es negativo (ni siquiera hay N0 i+), no realizar linfadenectomía. En caso de micrometástasis tras BSGC tras quimioterapia neoadyuvante, debería completarse la linfadenectomía.

B. CIRUGÍA

¿Qué opciones quirúrgicas de la mama existen?

¿En qué consiste la conservación de la mama?

¿Cuándo no se puede realizar la cirugía conservadora?

¿Cómo valorar los bordes quirúrgicos y qué hacer si están afectos?

¿Cuándo se realiza la mastectomía y que tipos hay?

¿Cómo y cuándo realizar la reconstrucción de la mama?

VER RESUMEN

2. Manejo locoregional

b) Cirugía. Tipos de cirugía: Cirugía conservadora

¿Qué opciones quirúrgicas de la mama existen?

Las dos intervenciones que se realizan son:

- **Cirugía conservadora**
- **Mastectomía**

¿En qué consiste la conservación de la mama?

CIRUGÍA CONSERVADORA (CC)

Es la recomendada como primera opción en las guias ESMO(20). En general es aplicable en tumores de hasta 3 cm y consiste en la extirpación del tumor sin llevarse excesivo tejido glandular normal; debe ir seguida de radioterapia (RT) para erradicar la posible enfermedad residual.

- El objetivo es ser una intervención equivalente a la mastectomía, con bajas tasas de recaída local y con un resultado cosmético aceptable.
- Todos los datos existentes, incluidos seis estudios aleatorizados y el metaanálisis de Oxford comparando CC con mastectomía, objetivan supervivencias equiparables (64).
- Se utiliza la **tumorectomía amplia**.

¿Cuándo no se puede realizar la cirugía conservadora?

Contraindicaciones

Las contraindicaciones para este tipo de cirugía son:

- Márgenes afectos persistentes tras unos intentos razonables de ampliación.
- Enfermedad multicéntrica o microcalcificaciones malignas difusas que la sugieren.
- Radioterapia previa (no se podrá irradiar) o embarazo.
- Contraindicaciones relativas:
  - Relación tamaño tumoral/tamaño de la mama
  - Esclerodermia y otras enfermedades reumáticas (toxicidad cutánea a la radioterapia)

¿Cómo valorar los bordes quirúrgicos y qué hacer si están afectos?

Bordes quirúrgicos

Márgenes libres:

No hay un consenso sobre qué distancia del tumor al margen de resección es necesaria para considerarlo libre, y aunque inicialmente se hablaba de 2 mm como margen libre de tumor microscópico, sin embargo, márgenes inferiores a 1-2 mm no modifican la supervivencia (65).

La revisión del panel de expertos de SSO/ASTRO en 2014 indica que el estándar para considerar un margen libre es **que no haya células tumorales adyacentes a cualquier borde o superficie de la pieza marcada con tinta**, que es el método que utiliza el cirujano para señalar los bordes de resección (66). En el caso de carcinoma in situ es preferible un margen de más de 2mm (60, 67-69).

Márgenes afectos:

La existencia de márgenes microscópicamente infiltrados implica un **aumento del riesgo de recidiva al doble**, y este aumento del riesgo no se elimina ni se reduce con una sobreimpresión de radioterapia, administración de terapia sistémica (endocrina, quimioterapia, terapia biológica) o biología favorable (66), aunque no modifica la supervivencia.

Por lo tanto, cuando existen márgenes afectos **se recomienda realizar ampliación quirúrgica de los mismos hasta conseguirlos libres**. Solo se indica sobreimpresión con radioterapia en caso de bordes irresecables (Ej. borde profundo/pectoral).

¿Cuándo se realiza la mastectomía y qué tipos hay?

MASTECTOMÍA

Los tipos de mastectomía son:

Mastectomía simple:

Es la intervención estándar de las mastectomías y consiste en **la extirpación completa de la mama y fascia del pectoral mayor**. Se denomina mastectomía radical modificada (MRM) cuando además incluye linfadenectomía axilar homolateral de niveles I y II.

Mastectomía ahorradora de piel/subcutánea:

- Incluye extirpación de todo el parénquima mamario, la piel por encima del tumor y cualquier cicatriz de biopsia. El procedimiento inicial también incluía la extirpación del complejo areola/pezón, aunque la experiencia actual indica que en pacientes seleccionadas (tumores periféricos y T1) podría preservarse, pero hay que tener en cuenta que esto significa dejar tejido mamario (un 5 %).
- La preservación de la piel de la mama y el bolsillo inframamario permite mucho mejores resultados cosméticos.
- Los datos actuales no apoyan un aumento del riesgo, pero estos datos son limitados (70).
- Algunos cirujanos la utilizan en estadios I y II con reconstrucción inmediata y en casos de mastectomías profilácticas.
- No precisan irradiación posterior complementaria.

¿Cómo y cuándo realizar la reconstrucción de la mama?

RECONSTRUCCIÓN MAMARIA

Las tasas de reconstrucción mamaria están aumentando de forma importante, en parte por el cambio de actitud tanto de las mujeres con cáncer de mama como de los médicos, así como el reconocimiento de los beneficios psicosociales obtenidos. En general, son las intervenciones de tipo mastectomía las que son susceptibles de reconstrucción, ya que la cirugía conservadora normalmente no lo requiere. Las guías ESMO indican que debe ser propuesta a todas las mujeres que requieren mastectomía (27).

Existen dos opciones:

- Implantes/prótesis
- Tejido propio: con colgajos (*flaps*) abdominales o dorsales

La reconstrucción puede ser:

- ***Inmediata:*** Parece no tener un impacto oncológico negativo y tiene la ventaja del beneficio emocional de reducir el impacto de perder el pecho. En la parte negativa, están las potenciales complicaciones de la mastectomía (infección, pérdida de piel) y de la radioterapia, si se precisa, que puede aumentar el grado de fibrosis, lo que influye negativamente en el resultado cosmético. La única razón que contraindica la reconstrucción inmediata es el carcinoma inflamatorio.
- ***Diferida:*** A partir de los seis meses de finalizar el tratamiento. También se plantean intervenciones correctoras de defectos parciales (*lipofilling*…)

C. RADIOTERAPIA

¿Qué beneficios tiene la radioterapia adyuvante?

¿Cómo valoro si una paciente requiere radioterapia?

¿Se puede omitir la radioterapia en pacientes con cirugía conservadora?

¿Cuándo irradiar a las pacientes con mastectomía?

¿Cambia la indicación de radioterapia si la paciente ha recibido quimioterapia neoadyuvante?

¿Cuándo dar sobreimpresión?

¿Cuáles son los tipos y dosis de la radioterapia?

VER RESUMEN
2. Manejo locorregional
c) Radioterapia

¿Qué beneficios tiene la radioterapia adyuvante?

BENEFICIOS

El metaanálisis de Oxford puso de manifiesto que la radioterapia tras cirugía conservadora o mastectomía **disminuye la recaída locorregional y mejora la supervivencia** (71).

¿Cómo valoro si una paciente requiere radioterapia?

INDICACIONES DE LA RADIOTERAPIA

Hay que valorar el tipo de cirugía (cirugía conservadora o mastectomía) y el riesgo de recidiva locorregional (hallazgos en el estudio de anatomía patológica a nivel ganglionar y el estado de los bordes):

A. Cirugía conservadora:

Indicación de radioterapia. Tasa de recidivas locales semejante a la mastectomía.

¿Se puede omitir la radioterapia en pacientes con cirugía conservadora?

- ***Mujeres mayores de 70 años, pT1, RH(+):*** Un **metaanálisis de cinco estudios aleatorizados publicado en *Annals of Surgical Oncology* (72)** pone de manifiesto en estas pacientes un ligero aumento de la recaída local (6,5 vs. 2,2 %), pero sin impacto en la recaída a distancia ni en la supervivencia global (SG).
- De la misma manera, **el ensayo Prime II (73)** también objetiva en mujeres ≥ 65 años con tumores T1-2 (hasta 3 cm) N0, RH(+) un ligero aumento de recaída local (3,2 vs. 0,8 %), pero sin afectar la supervivencia. Este efecto, se da sobre todo en pacientes con poca expresión de RH.
- Por todo esto, parece razonable **que en mujeres de estas características pudiera obviarse la radioterapia: *mujeres > 70 años, RH(+) y tratamiento con hormonoterapia adyuvante.***

B. Radioterapia posmastectomía inicial:

Desde la actualización del metaanálisis de Oxford en 2014, se considera la RT posmastectomía en pacientes con afectación ganglionar (incluidos uno a tres ganglios), ya que el metanálisis objetivó una falta de beneficio en SLP y SG para las pacientes N0, pero un beneficio claro para todas las pacientes con ganglios positivos (71).

Tabla 14. Metaanálisis de Oxford. Mortalidad y recaídas en mujeres de uno a tres ganglios positivos con mastectomía. Basada en Early Breast Cancer Trialists' Collaborative Group (EBCTCG) et al. (71).

1.ª recurrencia locorregional			Cualquier 1.ª recurrencia*			Mortalidad por Ca Mama**		
	%	p	%[1]	p	Riesgo relativo	%[2]	p	Riesgo relativo
NO RT	20,3	-	45,7	-		50,2		
RT	3,8	< 0,00001	34,2	0.00006	0,68 (IC 95 % 0,57 - 0,82)	42,3	0,01	0,80 (IC 95 % 0,67 - 0,95)

*1 % a los 10 años 2 % a los 10 años *Ganancia de 11.5 % a los 10 años ** Ganancia del 7.9 % a los 20 años*

¿Cuándo irradiar a las pacientes con mastectomía?

Según la actualización de las guias ASTRO presentadas en el San Antonio Breast Cancer Symposium 2017, es indicación de RT posmastectomía:

- N0: Todos los tumores T4.
- Pacientes pN2-3
- Márgenes infiltrados no resecables

En cuanto a los pacientes pN1, indica que los ensayos objetivan una disminución de la recaída locorregional y de la mortalidad, pero que la indicación debe sentarse en un comité multidiciplinar y de acuerdo con las caracterisiticas de los pacientes, valorando riesgos, factores de riesgo (**Tabla 15**) y beneficios. Lo mismo sucede en el caso de los pacientes con tumores pT3 con algún factor de riesgo.

Por otra parte no existe evidencia ni a favor ni en contra de la RT si la biopsia del ganglio centinela es positiva y no se realiza linfadenectomía.

Tabla 15. Factores de riesgo. Guías Astro .

RIESGO recaída locorregional	BAJO (< 10 %)	INTERMEDIO / ALTO (>10-20 %)
Edad		< 40 años
Grado	1-2	3
Invasión vasculo-linfática	No	Si
Histología	Ductal	Lobulillar

¿Cambia la indicación de radioterapia si la paciente ha recibido quimioterapia neoadyuvante?

C. Radioterapia posmastectomía tras quimioterapia neoadyuvante:

La evidencia actual indica que hay que irradiar en el estadio III inicial aunque haya una respuesta completa, y también en los tumores T3.

No hay evidencia en el beneficio de la radioterapia en los N1 de inicio que tras la quimioterapia son N0, por lo que se irradian, a la espera de los resultados de ensayos clínicos en marcha (NSABP B51 (74), ALLIANCE A011202 (75) (aún pendiente de los resultados).

En conclusión: ***hay que irradiar en función del estadio previo a la quimioterapia***

¿Cuándo dar sobreimpresión?

D. Sobreimpresión (boost):

El seguimiento a 20 años del **ensayo fase III de la EORTC** (76, 77) sigue evidenciando una disminución de las recaídas sin efecto sobre la supervivencia y mayor toxicidad en forma de fibrosis, pero cuando se analiza por grupos de edad se ve que las mujeres jóvenes presentan mayor beneficio.

Tabla 16. Recaídas EORTC 10801. ***Basada en Bartelink H. et al. (77).***

Grupo Edad	Boost	No boost	Hazard Ratio	p
≤ 40 años	71 recurrencias	41 rec.	0,56 (IC 99 % 0,34 - 0,92)	0,003
41-50 años	108 recurrencias	74 rec.	0,66 (IC 99 % 0,45 - 0,98)	0,007
51-60 años	100 recurrencias	64 rec	0,69 (IC 99 % 0,46 - 1.04)	0,020
> 60 años	75 recurrencias	57 rec	0,66 (IC 99 % 0,42 - 1.04)	0,019

Las guías ASTRO actualizadas en 2018 (78) recomiendan su utilización cuando se cumpla alguno de los siguientes criterios:

- Mujeres menores de 50 años
- Mujeres entre 51 y 70 años con tumores de alto grado
- Márgenes positivos

Podría obviarse en mujeres > 70 años con tumores RH(+), G1/2 con márgenes > de 2 mm.

¿Cuáles son los tipos y dosis de la radioterapia?

DOSIS Y FRACCIONAMIENTO

A. Fraccionamiento estándar:

Radioterapia externa

- Acelerador lineal (o cobaltoterapia).
- Dosis de 45-50 Gy con fraccionamiento de 2 Gy/día durante 5 semanas.

Sobreimpresión o "Boost"

- Electrones (radioterapia externa): 5-8 sesiones hasta alcanzar 56/66 Gy de dosis total
- Braquiterapia:
  - Alta tasa (1 sesión)
  - Baja tasa (ingreso de 2 días)

Hipofraccionamiento:

- Permite acortar la duración del tratamiento a tres semanas.
- En mujeres con cáncer de mama invasivo que reciben radioterapia de mama entera con inclusión o no de la axila inferior, se recomiendan dosis de 4000 cGy en 15 fracciones o 4250 en 16 fracciones(78). Los ensayos aleatorizados de hipofraccionamiento con resultados a más de 10 años demuestran l**a equivalencia con el estándar** (79) **siendo una alternativa segura y efectiva**. 2 metanálisis (80, 81) demuestran que **no existen diferencias en recaída locoregional, supervivencia ni resultado estético a largo plazo y se relaciona con menor toxicidad aguda. La dosis recomendada por fracción sería la de 2.5 - 3.0 Gy.**

B. Irradiación parcial de la mama (IPM):

- Es la irradiación solo de la parte de la mama donde se localizaba el tumor.
- Es **una aproximación en investigación**: los últimos estudios aleatorizados muestran una tasa de recurrencia local baja pero significativamente mayor que la de la irradiación total (4,4 vs. 0,4 y 3,3 vs. 0,3 %) y estos datos se confirman en un **metaanálisis (82)**. Existen ensayos aleatorizados en marcha que le darán a la IPM su verdadero papel.
- Se realiza de forma perioperatoria, generalmente con braquiterapia de alta tasa.
- La actualización de los criterios de la ASTRO, presentada en el congreso de San Antonio de 2017, consensua que se puede utilizar en pacientes seleccionados de buen pronóstico que cumplen los siguientes criterios:
  - Mujeres ≥ 50 años
  - Sin mutación BRCA 1/2
  - CDI (no Carcinoma lobulillar infiltrante (CLI))
  - T1 y Tis (CDis)
  - No multicéntrico. Multifocal sí, pero < de 2 cm globalmente
  - Márgenes libres > 2 mm
  - Cualquier grado pero sin infiltración vasculo-linfática
  - RH positivos
  - Ganglios negativos (pN0)
  - No indicación de quimioterapia neoadyuvante

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