

Cardiotoxicidad en el tratamiento del cáncer

XII CURSO DE FISIOPATOLOGÍA CARDIOVASCULAR DEL SÍNTOMA A LOS GENES

30 de noviembre y 1 de diciembre de 2018

Centro Nacional de Investigaciones
Cardiovasculares (CNIC)



Documentos de consenso en Cardio-Oncología

¿Dónde estamos? ¿Qué nos falta?



Teresa López Fernández

Cardio-Oncología: ¿Dónde estamos?



European Heart Journal (2016) 37, 2768–2801
doi:10.1093/eurheartj/ehw211

ESC CPG POSITION PAPER

2016 ESC Position Paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC Committee for Practice Guidelines

The Task Force for cancer treatments and cardiovascular toxicity of the European Society of Cardiology (ESC)

Authors/Task Force Members: Jose Luis Zamorano* (Chairperson) (Spain), Patrizio Lancellotti* (Co-Chairperson) (Belgium), Daniel Rodriguez Muñoz (Spain), Victor Aboyans (France), Riccardo Asteggiano (Italy), Maurizio Galderisi (Italy), Gilbert Habib (France), Daniel J. Lenihan¹ (USA), Gregory Y. H. Lip (UK), Alexander R. Lyon (UK), Teresa Lopez Fernandez (Spain), Dania Mohty (France), Massimo F. Piepoli (Italy), Juan Tamargo (Spain), Adam Torbicki (Poland), and Thomas M. Suter (Switzerland)

European Heart Journal (2016) 37, 2768–2801



Sociedad Española de Hematología y Hemoterapia



Artículo especial

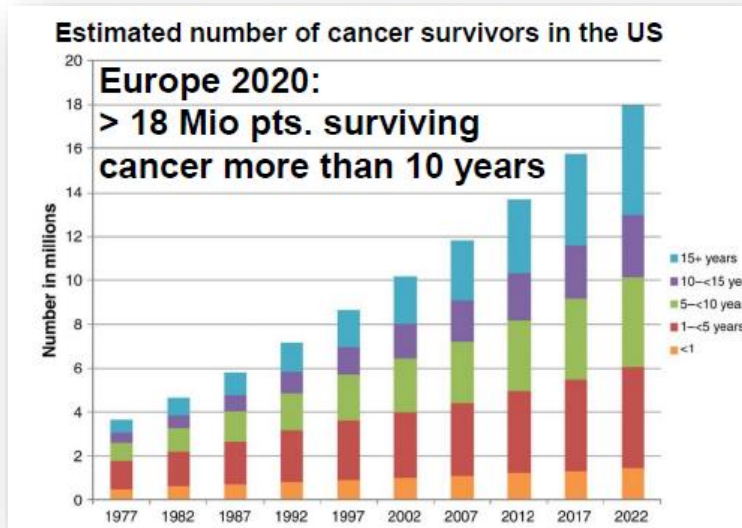
Cardio-Onco-Hematología en la práctica clínica.
Documento de consenso y recomendaciones



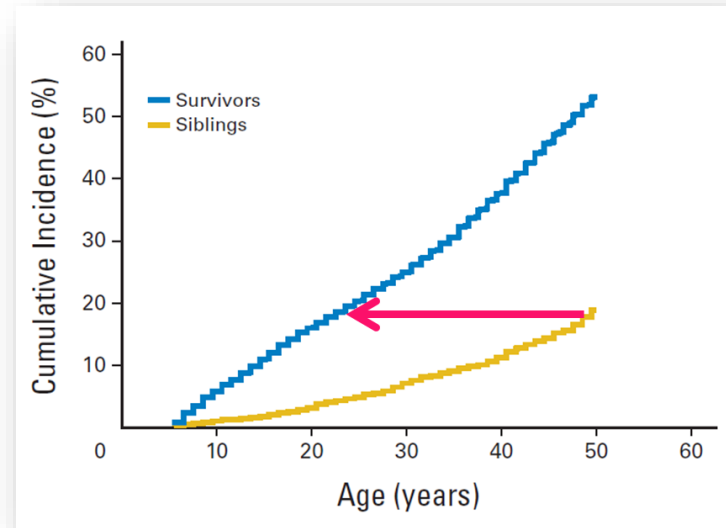
Teresa López-Fernández^{a,b,*}, Ana Martín García^{b,c}, Ana Santaballa Beltrán^{b,d}, Ángel Montero Luis^{b,e}, Ramón García Sanz^{b,f}, Pilar Mazón Ramos^g, Sonia Velasco del Castillo^h, Esteban López de Sá Areses^a, Manuel Barreiro-Pérez^c, Rocío Hinojar Baydesⁱ, Leopoldo Pérez de Isla^l, Silvia Cayetana Valbuena López^a, Regina Dalmau González-Gallarza^a, Francisco Calvo-Iglesias^k, Juan José González Ferrer^{b,j}, Antonio Castro Fernández^l, Eva González-Caballero^m, Cristina Mitro^{b,n}, Meritxell Arenas^{b,o}, Juan Antonio Virizuela Echaburu^{b,p}, Pascual Marco Vera^{b,q}, Andrés Íñiguez Romo^k, José Luis Zamorano^{i,1}, Juan Carlos Plana Gómez^{r,1} y José Luis López Sendón Henchel^{a,1}

Rev Esp Cardiol 2017;70:474–86.

Cardio-Oncología: ¿Dónde estamos?

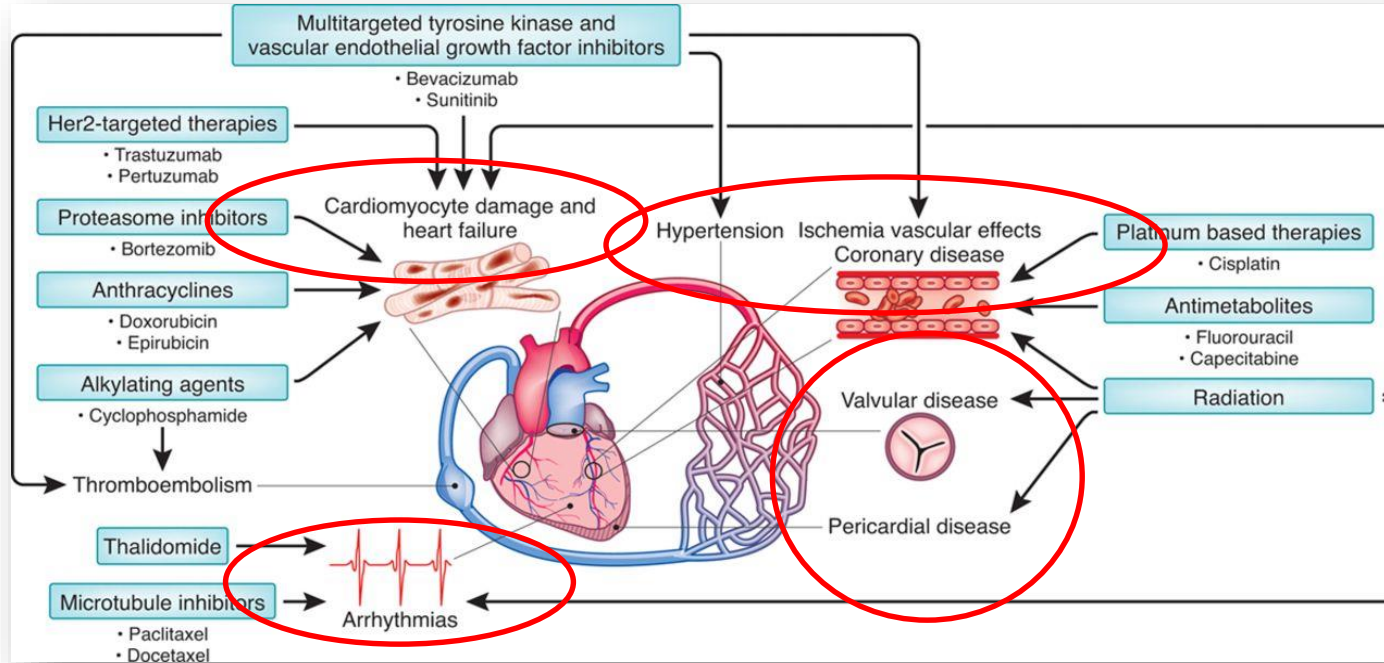


de Moor J et al. Cancer Epid Biomarkers Prev 2013; 22:561-570

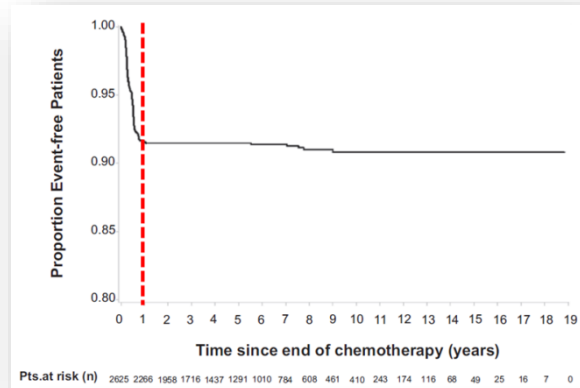


mod. Armstrong GT et al. J Clin Oncol. 2013 Oct 10;31(29):3673-80.

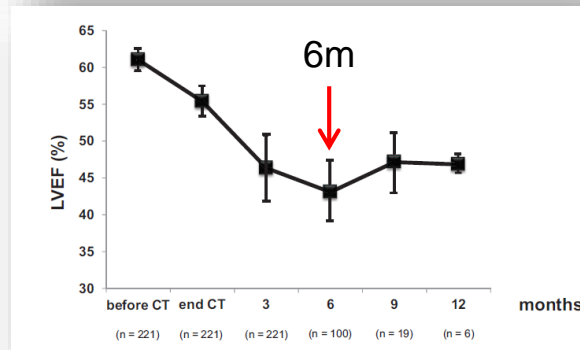
Impacto del tratamiento del cáncer en el sistema CV



Impacto del tratamiento del cáncer en el sistema CV



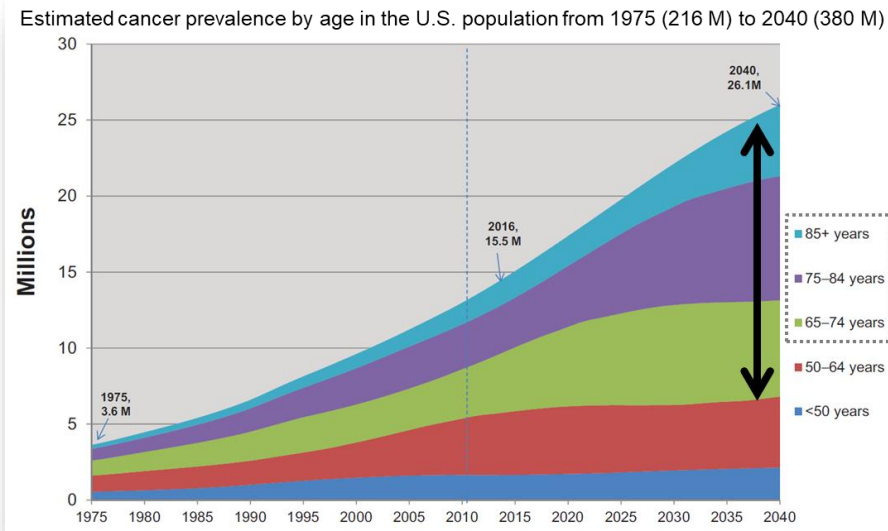
2625 pacientes: **9%CTox**
→ **98% en el 1er año**
→ **81% NYHA I-II**



↓ **Opciones terapéuticas**
↑ **Mortalidad oncológica**

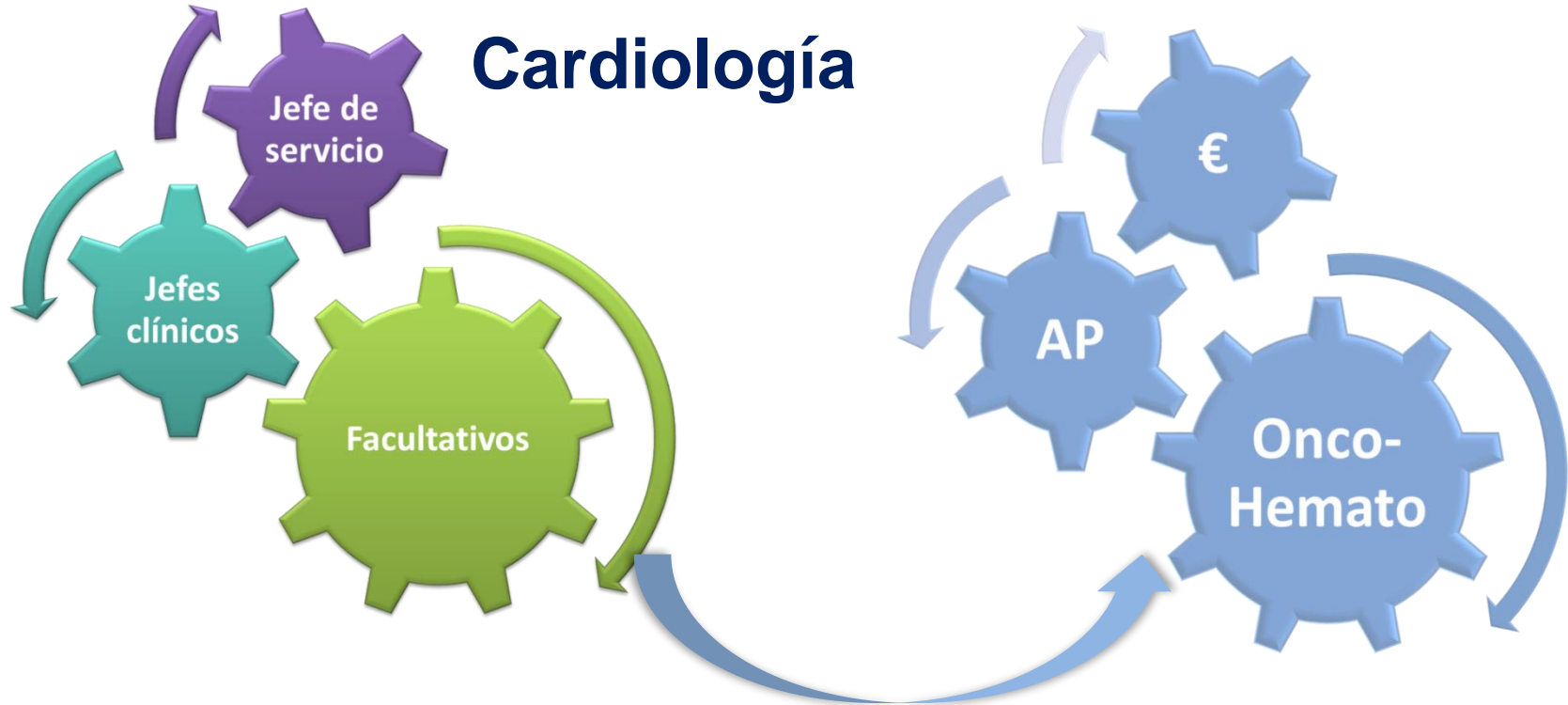
Circulation. 2015;131:1981-1988

Cardio-Oncología: ¿Dónde estamos?



- 2/3pp >65 años
- Comorbilidades
- 30% ECV
- Ttos prolongados

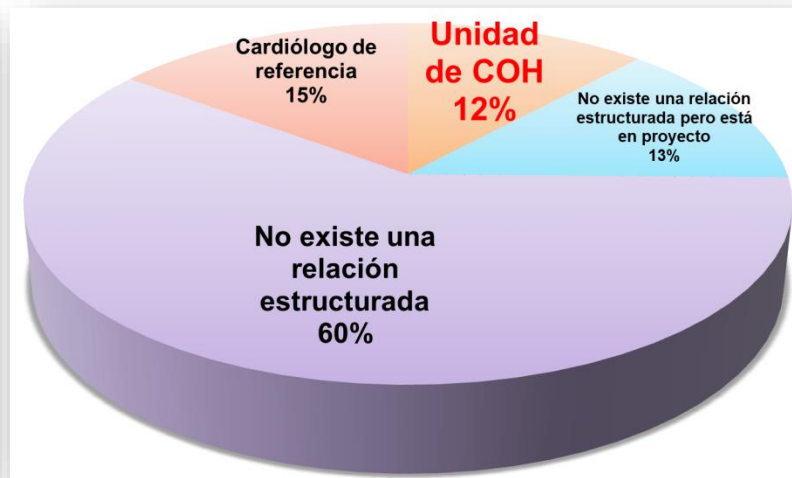
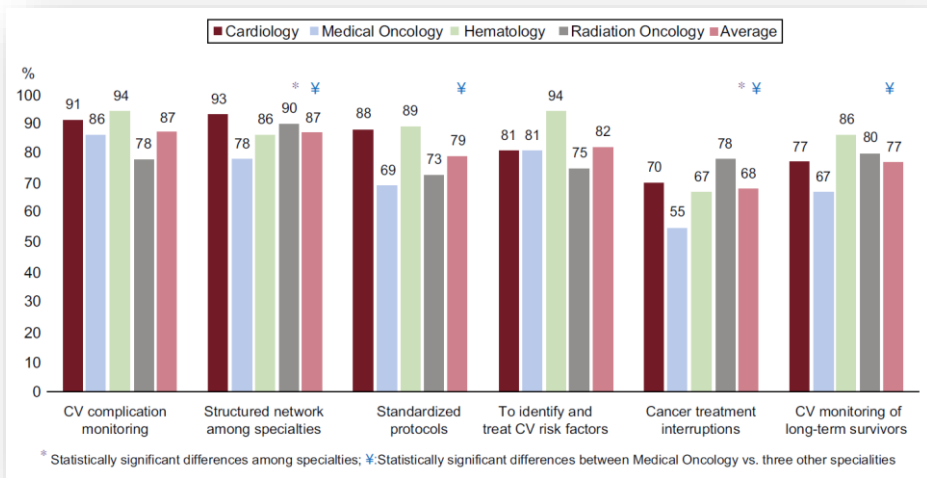
Cardio-Oncología: ¿Dónde estamos?



Situación actual de la Cardio-Oncología en España



Sociedad Española de Hematología y Hemoterapia



Rev Esp Cardiol 2017. DOI: 10.1016/j.recesp.2017.10.051

Reto n° 1

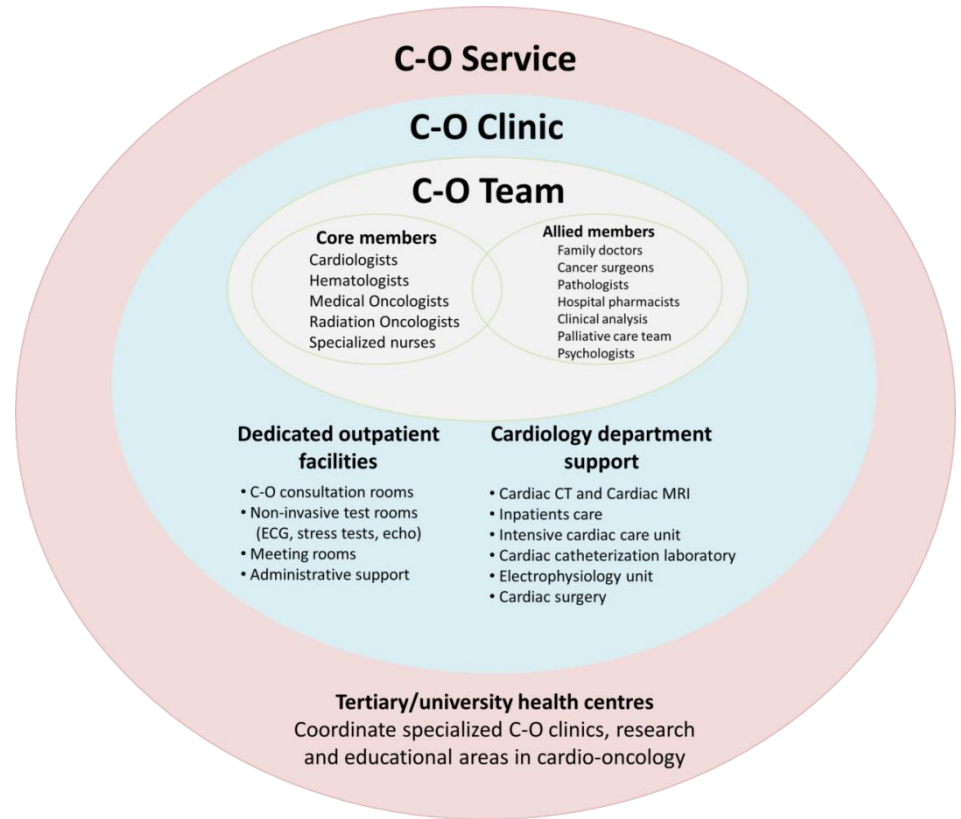
Equipos de Cardio-Oncología

Cardio-Oncology Services: rationale, organization, and implementation

A report from the ESC Cardio-Oncology council

Patrizio Lancellotti^{1,2*}, Thomas M. Suter³, Teresa López-Fernández⁴, Maurizio Galderisi⁵, Alexander R. Lyon⁶, Peter Van der Meer⁷, Alain Cohen Solal⁸, Jose-Luis Zamorano⁹, Guy Jerusalem¹⁰, Marie Moonen¹, Victor Aboyans¹¹, Jeroen J. Bax¹², and Riccardo Asteggiano¹³

European Heart Journal (2018) 00, 1–8



Equipos de Cardio-Oncología

Engagement of staff	<ul style="list-style-type: none">• Cardiologist (general, heart failure specialist, cardio-oncology specialist, fellows)• Nurse• Administrative staff
Definition of services	<ul style="list-style-type: none">• Baseline evaluation; on-treatment monitoring; cardiotoxicity management; long-term follow-up• Pre-operative evaluation• Cardiac tumour evaluation
Definition of referral criteria	<ul style="list-style-type: none">• High-risk patients; high-risk cancer therapy• History of cardiotoxicity• New cardiotoxicity during cancer therapy
Definition of on-treatment monitoring strategies	<ul style="list-style-type: none">• Modalities (clinical, biomarkers, imaging)• Timing
Definition of intervention strategies	<ul style="list-style-type: none">• Primordial prevention (before cancer therapy, in the absence of any abnormality)• Primary prevention (during cancer therapy; in the presence of subtle dysfunction)• Secondary prevention (during or after cancer therapy; in the presence of overt dysfunction)
Definition of long-term surveillance strategies	<ul style="list-style-type: none">• Modalities (clinical, biomarkers, imaging)• Timing
Establishment of collaborations and network	<ul style="list-style-type: none">• Medical Oncologist; Haematologist; Radiation Oncologist; Internist; other physicians• Cardiac imaging Specialist; Interventional Cardiologist; Electrophysiologist; In-patient cardiology unit• Home-care service; Psychosocial services

Farmakis D et al. Eur J Heart Failure (2018) doi:10.1002/ejhf.1336

Equipos de Cardio-Oncología

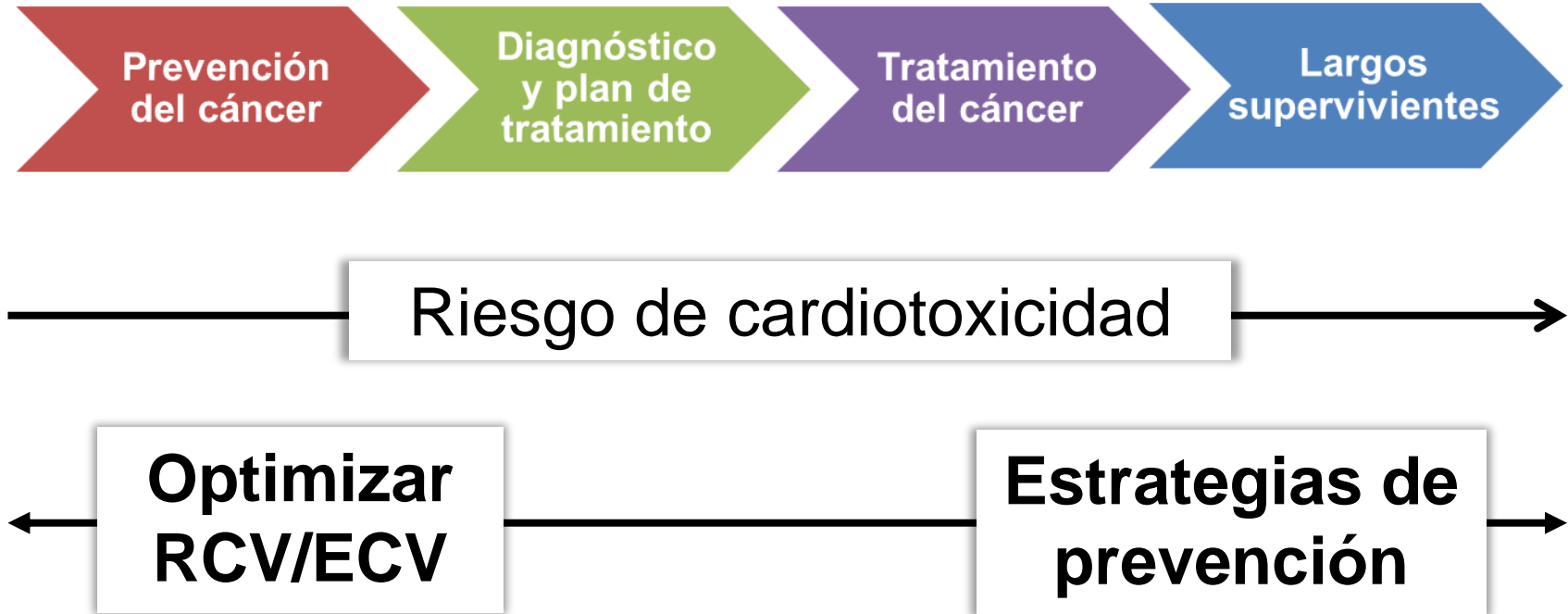


1. Facilitar el tratamiento del cáncer

- Minimizar interrupciones del tratamiento
- Mejorar la salud CV de pacientes oncológicos

2. Promover la educación e investigación

Cardio-oncología



Prevención CV = Prevención cáncer y CTox

www.mimocardio.org

mimocardio Cardio-oncología
cáncer

Cardio-oncología

¿Qué es la Cardio-Oncología?
Es el cuidado multidisciplinar de la salud cardiovascular en los pacientes con cáncer

mimocardio Cardio-oncología
cáncer
Cuida el corazón de los pacientes con cáncer

oncología médica
oncología radioterapéutica
cardiología
hematología

La coordinación entre cardiólogos, oncólogos, hematólogos y oncólogos radioterapeutas permite el cuidado global del paciente.

SEOM Sociedad Española de Oncología Médica
SEOR Sociedad Española de Oncología Radioterapéutica
SEH Sociedad Española de Hematología

mimocardio Cardio-oncología
cáncer

Buenas noticias ¡Se puede prevenir!

¿Cómo?

- **Estilo de vida Saludable**
Ejercicio físico + Dieta Saludable
- **Controlar factores de riesgo cardiovascular y mantener tratamiento cardiológico**

DIETA
No es el momento de perder peso pero sí de cambiar hábitos

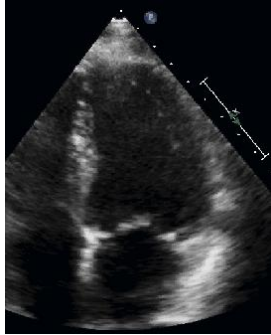
CONTROL
NO FUMAR
Controlar tensión arterial e hipercolesterolemia

EJERCICIO FÍSICO
Recomendaciones
150min SEMANALES
INTENSIDAD MODERADA
30min DIARIOS
5 días SEMANA

Reto nº 2

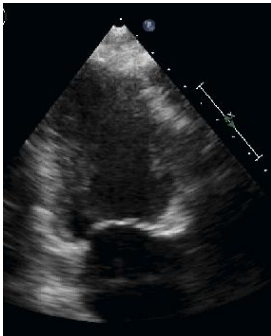
¡¡Definiciones!!

Crterios uniformes de Dx de DV-CTOX



↓ FEVI >10% con FEVI < 53%

J Am Soc Echocardiogr 2014;27:911-39; Can J Cardiology 2016; 32:831-841; Rev Esp Cardiol 2017;70:474-86



↓ FEVI >10% con FEVI < 50%

European Heart Journal (2016) 37, 2768-2801

FEVI-2D: variabilidad 8-11%

Criteria uniformes de Dx de DV-CTOX

↓ FEVI >10% con FEVI < 53%

J Am Soc Echocardiogr 2014;27:911-39; Can J Cardiology 2016; 32:831-841; Rev Esp Cardiol 2017;70:474-86

↓ FEVI >10% con FEVI < 50%

European Heart Journal (2016) 37, 2768-2801

SUCCOUR trial: cardiotoxicity definitions

Incidence

↓EF >0.10 from baseline to <0.55	or a relative ↓GLS by >12%	42%patients (46/108)
↓EF >0.10 from baseline to <0.53	or a relative ↓GLS by >15%	25%patients (28/108)

JACC Cardiovasc Imaging 2018, 11(8):1109-1118.



HFA

European Society of Cardiology



HFA Cardio-Oncology Biomarkers Workshop

Role of biomarkers in diagnosis and surveillance of cardiotoxicity in cancer patients receiving cardiotoxic therapies

HFA Cardio-Oncology Imaging Workshop

Role of cardiac imaging in diagnosis and surveillance of cardiotoxicity in cancer patients receiving cardiotoxic therapies

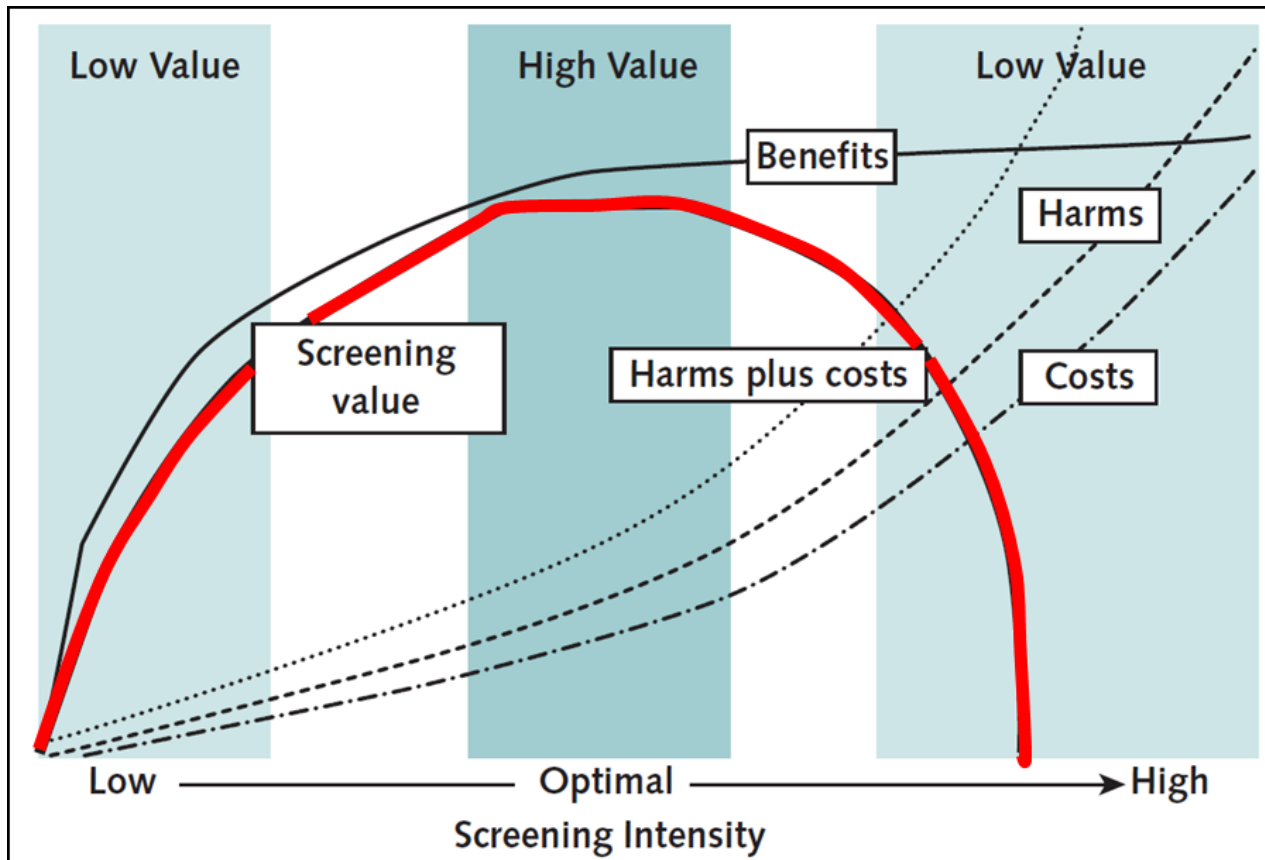
Table 2 Management strategies and percentage of patients completing cardiotoxic cancer therapy according to Royal Brompton Hospital myocardial toxicity class

Cardiotoxicity group	Classification	Definition	Management strategies	
			Oncology therapy	Cardiology therapy
1 	Early biochemical cardiotoxicity	New BNP or troponin I rise but with normal cardiac imaging. (If normal at baseline, then any increase above the upper limit of normal. If abnormal at baseline, then 20% rise).	Continue	Cardio-oncology review. Consider closer monitoring, or start low-dose ACEI or BB cardioprotection.
2	Early functional cardiotoxicity	New reduction in GLS or grade III–IV diastolic dysfunction and normal biomarkers.	Continue	Cardio-oncology review. Consider closer monitoring, or start low-dose ACEI or BB cardioprotection.
3	Early mixed cardiotoxicity	Normal LVEF with abnormal biomarkers and GLS/diastolic dysfunction.	Continue	Cardio-oncology review. Start low-dose ACEI or BB cardioprotection.
4 	Symptomatic HFpEF	Symptomatic HFpEF.	Interrupt and review risk/benefit*	Cardio-oncology review. Diuretic for fluid congestion. ACEI or BB cardioprotection if continuing cancer therapy.
5	Asymptomatic LVSD	New LVEF reduction to <50%, or a reduction in LVEF >10% to a LVEF <55% [†] .	Review and balance risk/benefit*	Cardio-oncology review. Start ACEI and/or BB and up-titrate to 50–100% target dose for HF as tolerated.
6	Symptomatic LVSD	Symptomatic reduction in LVEF <50%, or a reduction in LVEF >10% to a LVEF <55% [†] .	Interrupt and review risk/benefit*	Cardio-oncology review. Start ACEI and/or BB and up-titrate to 100% target dose for HF as tolerated ^{†#} .

PareekN....Lyon AR. European Journal of Heart Failure (2018)

Reto n° 3

Monitorización Scores de riesgo Prevención



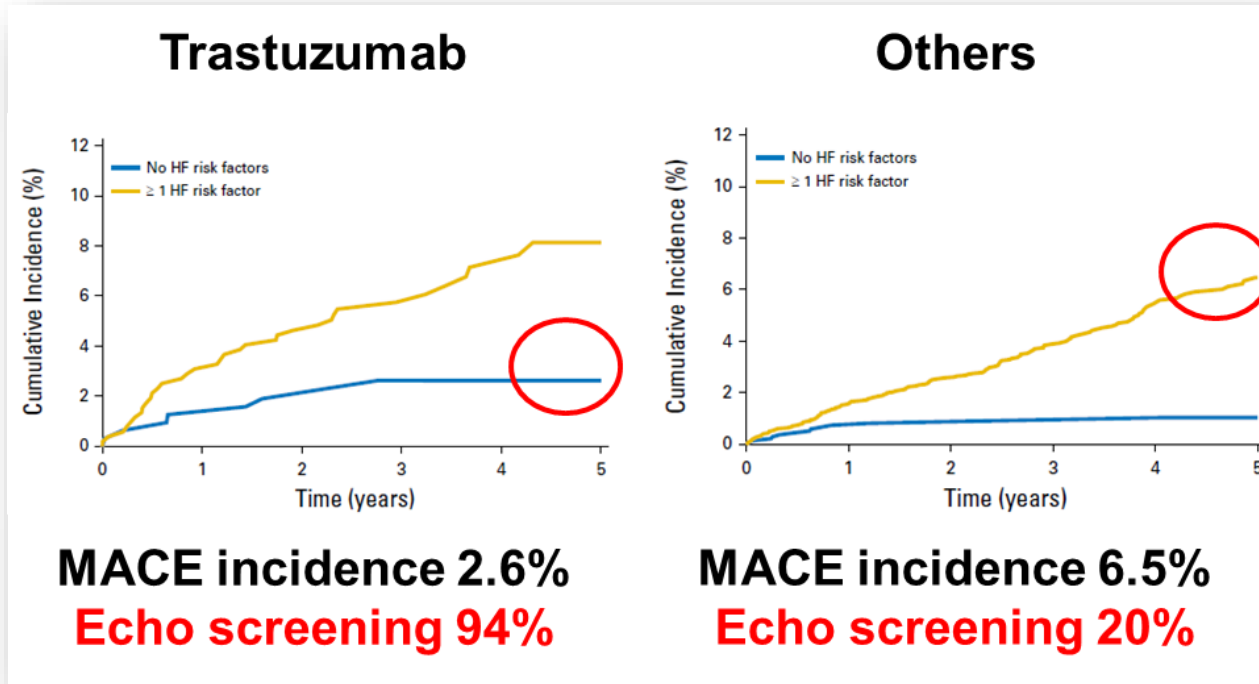
Ann Intern Med. 2015;162:712-717

No protocolos estandarizados de monitorización

	Stage A Risk Stratification and Modification	Stage B Screening for LV Dysfunction	Stage C Symptomatic HF	Stage D Advanced HF
Cancer Therapeutics				
Anthracyclines	✓	✓	✓	✓
HER-2 Therapy	✓	✓	✓	✓
VEGF Inhibitors	✓*	✓*	✓	○
Proteasome Inhibitors	○	○	✓	○
Immune Checkpoint Inhibitors	○	○	✓	○

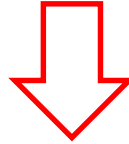
Kenigsberg B et al. JACC Heart Fail. 2018 Feb;6(2):87-95.

No protocolos estandarizados de monitorización



Thavendiranathan P et al J Clin Oncol 2018 May 23;JCO2018779736

¡¡Score de riesgo de CTOX!!



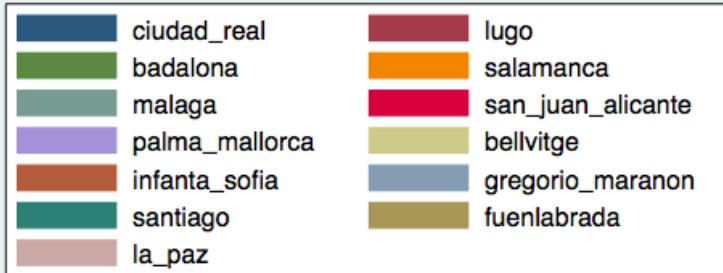
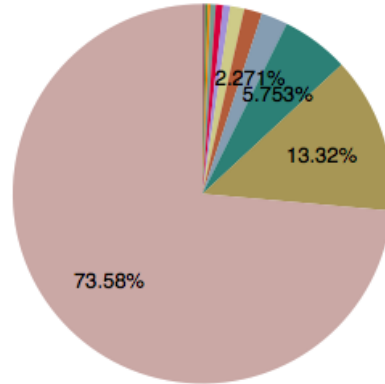
IdiPAZ
Instituto de Investigación
Hospital Universitario La Paz

ClinicalTrials.gov NCT02039622

Pacientes incluidos por hospital

Inclusión
2010-2017

Fin seguim
2019



ClinicalTrials.gov NCT02039622

1321 pacientes

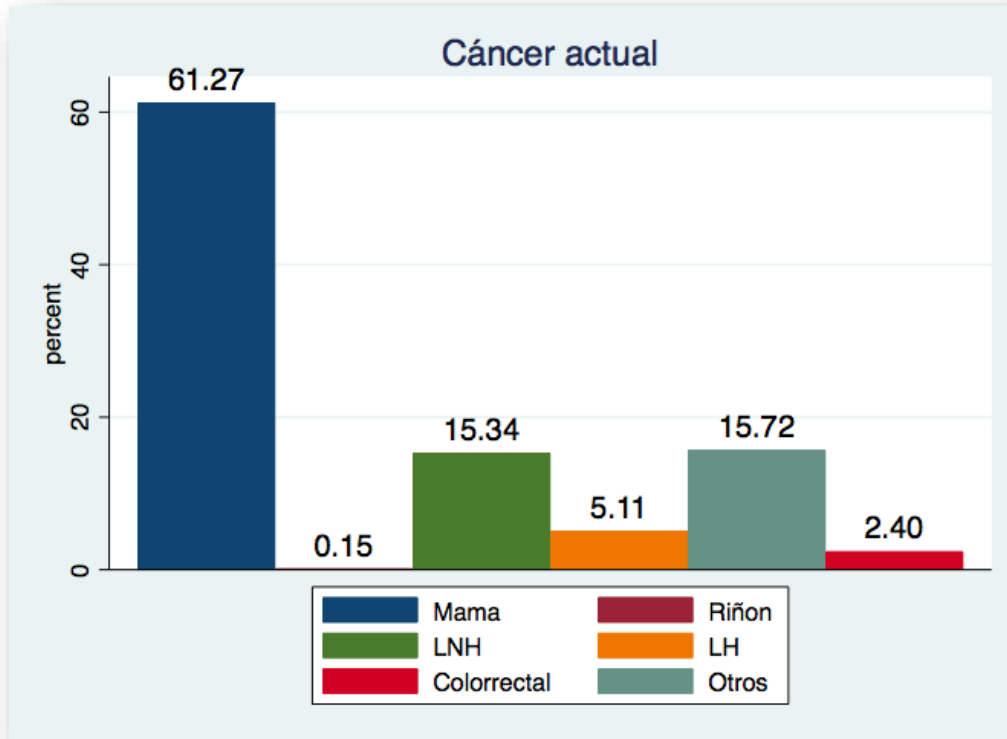
Edad media 55.3 años

80% mujeres

Mort anual 6.5%

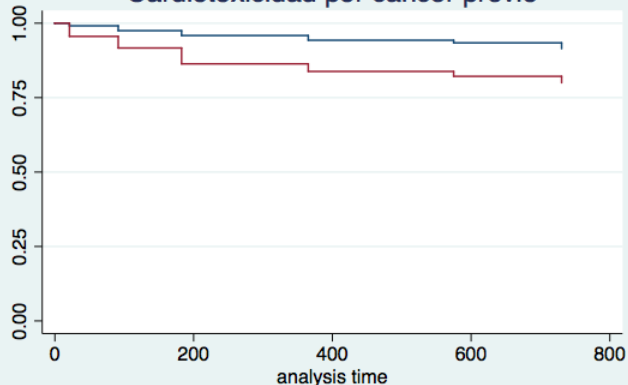


ClinicalTrials.gov NCT02039622



9.7% Ca previo
10% ECV previa
30% FRCV

Cardiotoxicidad por cáncer previo

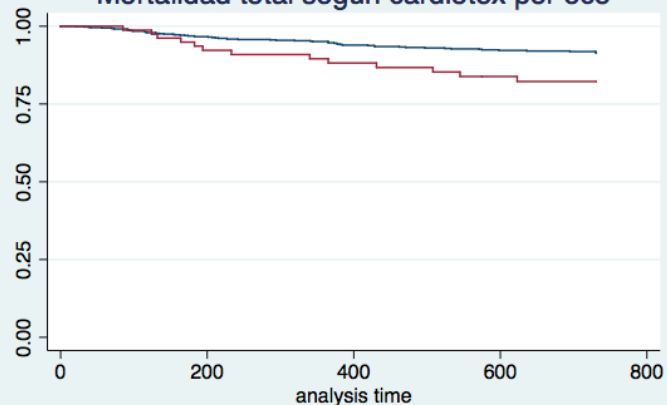


Number at risk

	0	200	400	600	800
ca_previo = No	1031	790	648	522	0
ca_previo = Sí	113	68	51	38	0

— ca_previo = No — ca_previo = Sí

Mortalidad total según cardiotox por eco

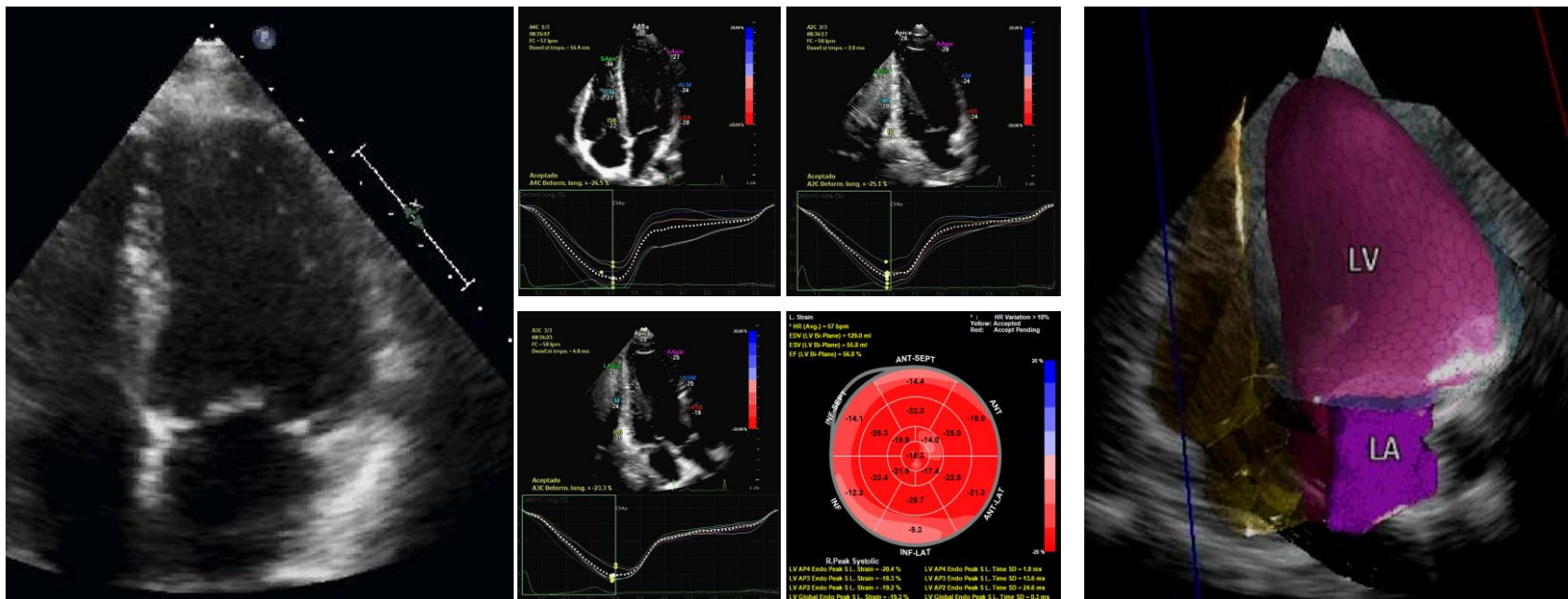


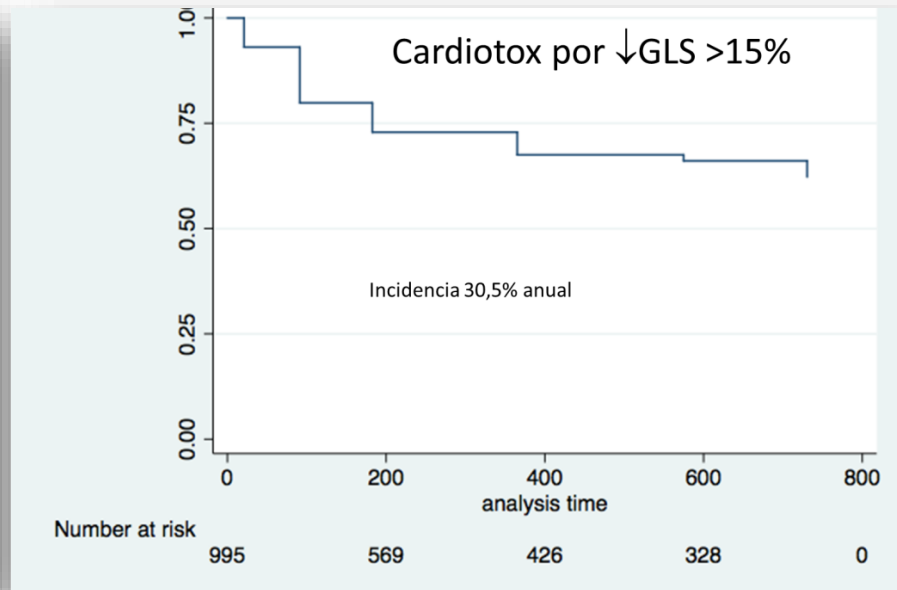
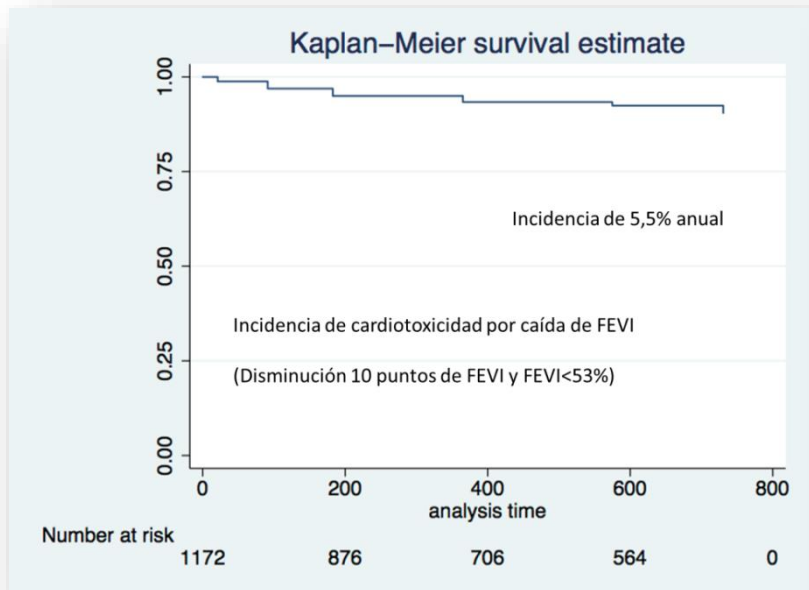
Number at risk

	0	200	400	600	800
cx_sv = 0	936	742	619	494	0
cx_sv = 1	79	68	61	52	0

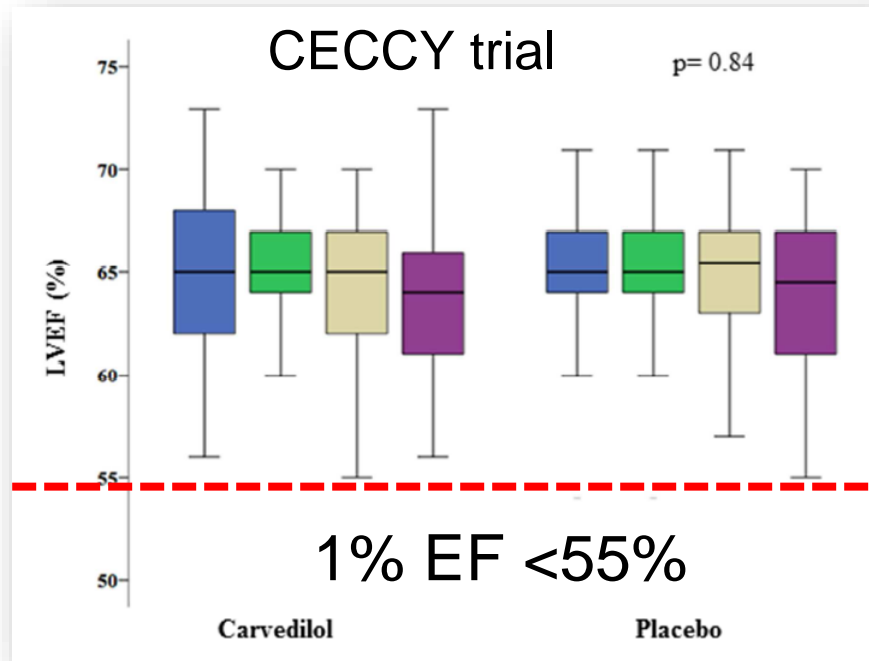
— No cardiotox — Sí Cardiotox

¿Qué elijo? 2D/3D/Strain/Troponina





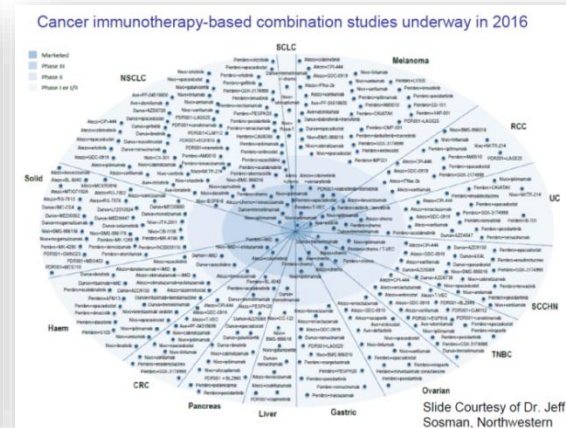
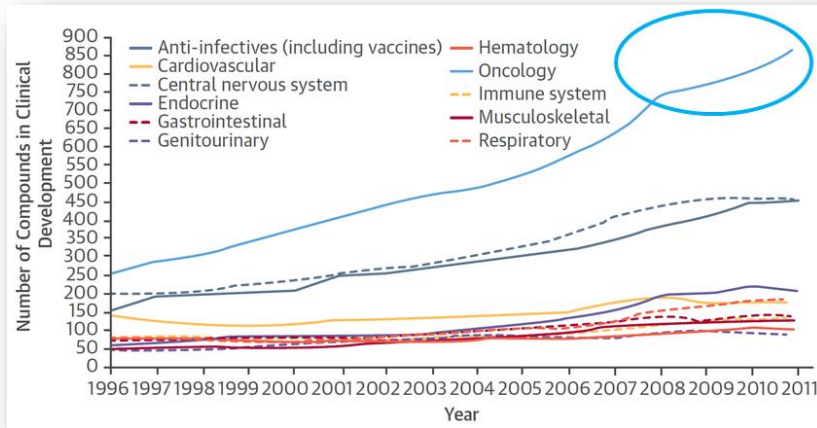
Prevención primaria de cardiotoxicidad



Avila MS et al. JACC(2018), doi: 10.1016/j.jacc.2018.02.049.

Reto n° 4

Investigación clínica

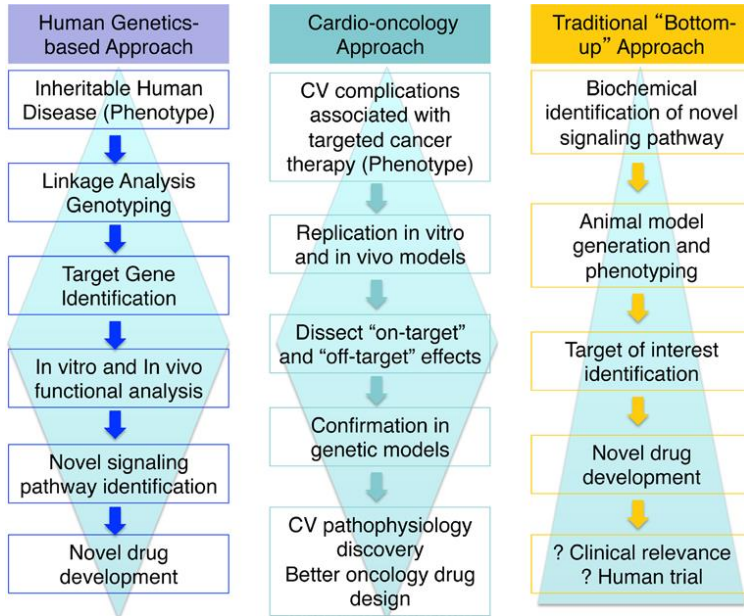


Cardiólogos en el diseño de ensayos en onco-hematología

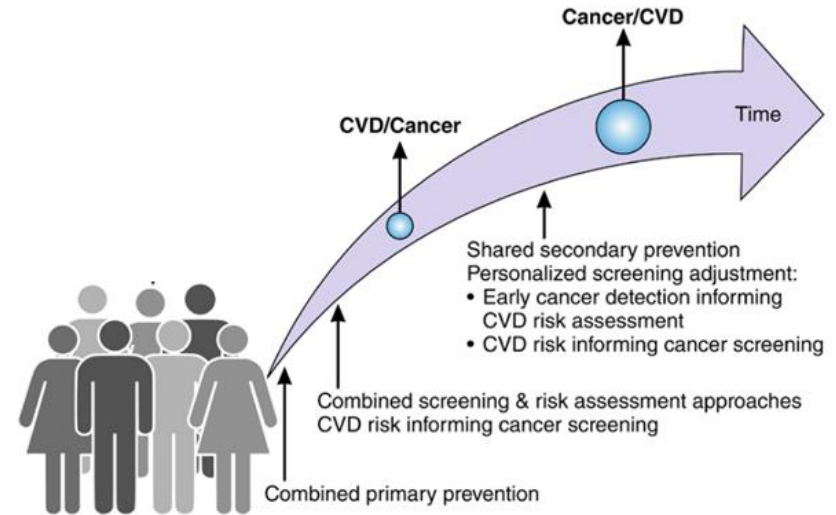
J Am Coll Cardiol 2015;65:1567–82

Reto nº 4

Investigación básica



Circulation. 2015;132:2248-2258

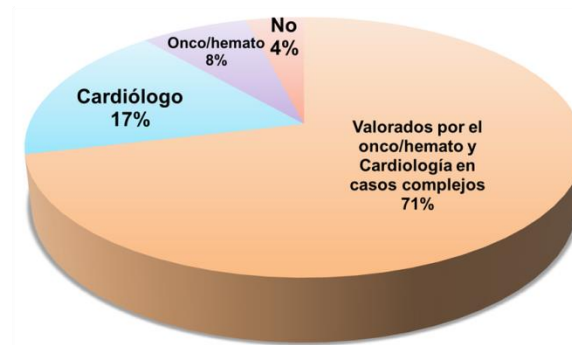


Circulation. 2018;138:727-734.

Reto n° 5

Formación

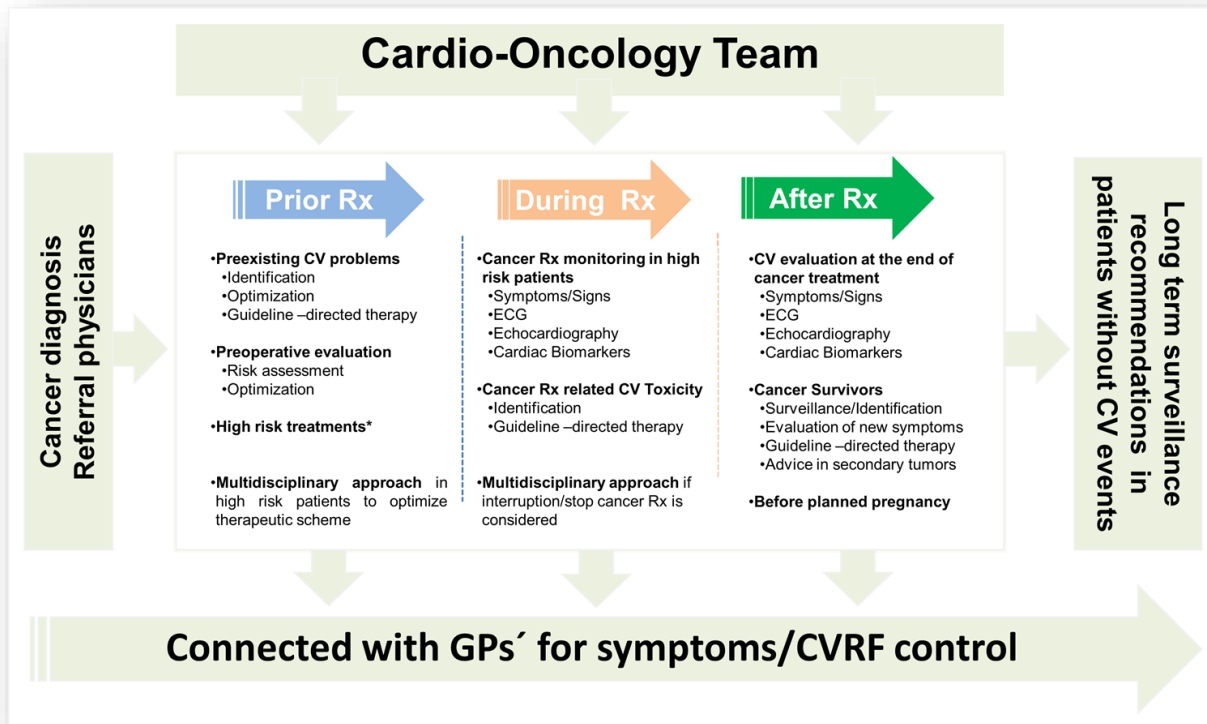
Valoración basal de los pacientes con cáncer y tratamiento cardiotóxico



80% evaluación basal por Onco/Hemato

Rev Esp Cardiol 2017. DOI: 10.1016/j.recesp.2017.10.051

Prioridades: Continuidad asistencial



European Heart Journal (2018) 00, 1–8

Prioridades: Continuidad asistencial



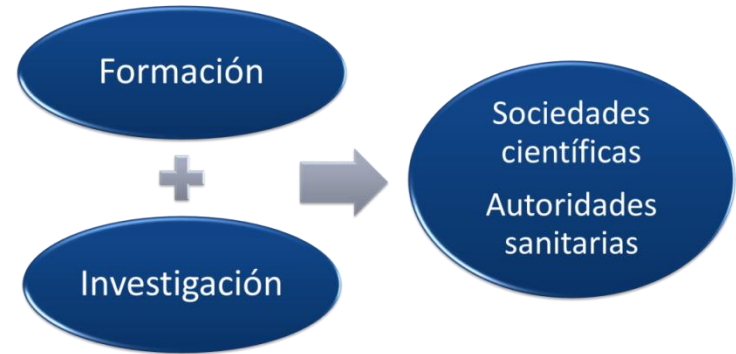
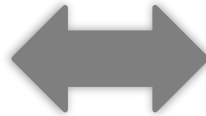
Sección de
Cardiología
Clínica

Grupo de
Cardio-oncología

SEC- Primaria

PROCESO CARDIO-ONCO-HEMATOLOGÍA (COH)

Los retos para el cardiólogo de la terapia oncológica



Grupo de
Cardio-oncología

<https://secardiologia.es/cientifico/grupos-de-trabajo/cardio-oncologia>



CardioTox 2019: Presente y futuro de la Cardio-Oncología

Fechas: 20-21 marzo 2019

Sede: Aula Ortiz Vázquez. H. Universitario La Paz

Directores: José Luis López Sendón; Teresa López-Fernández



Muchas gracias