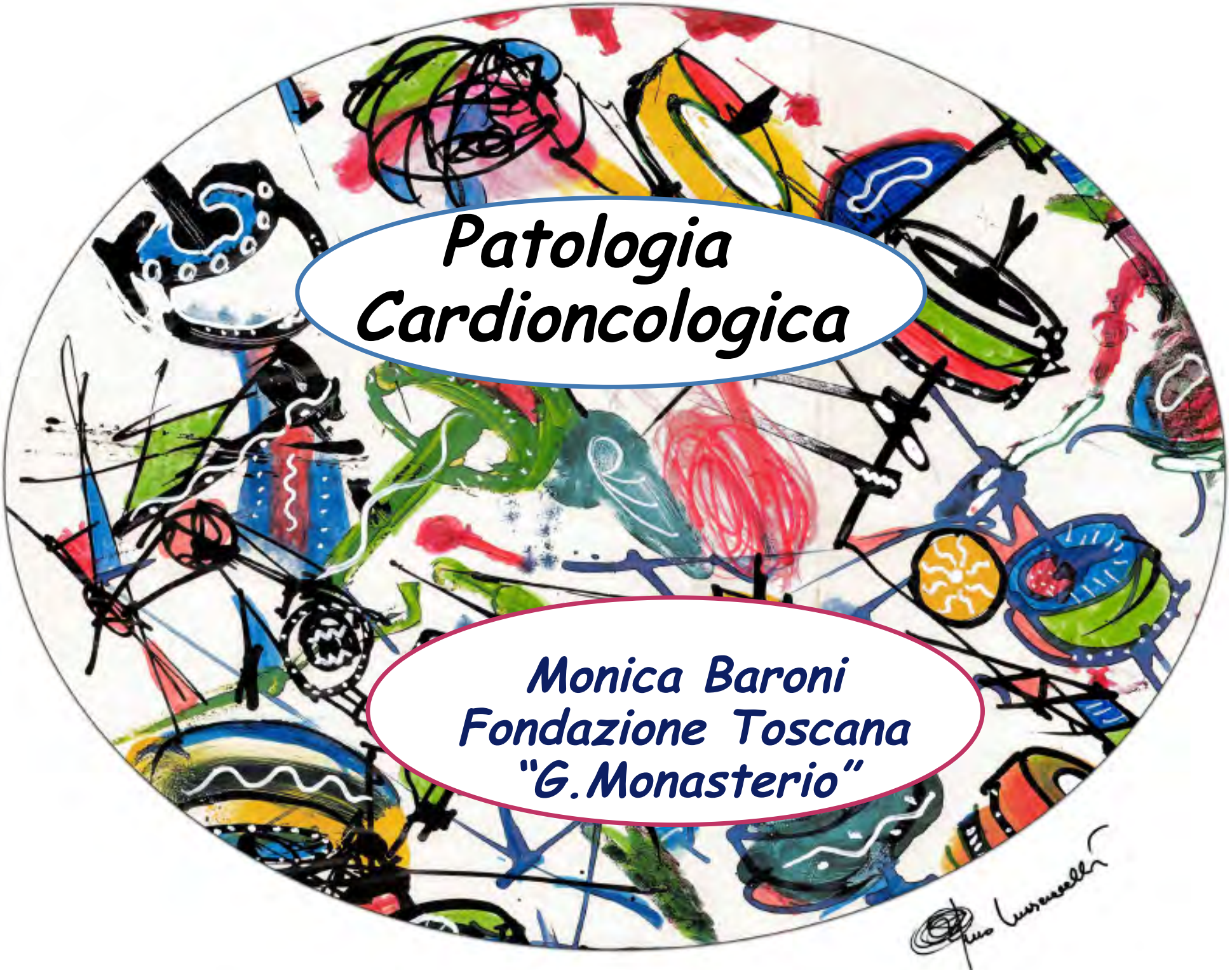
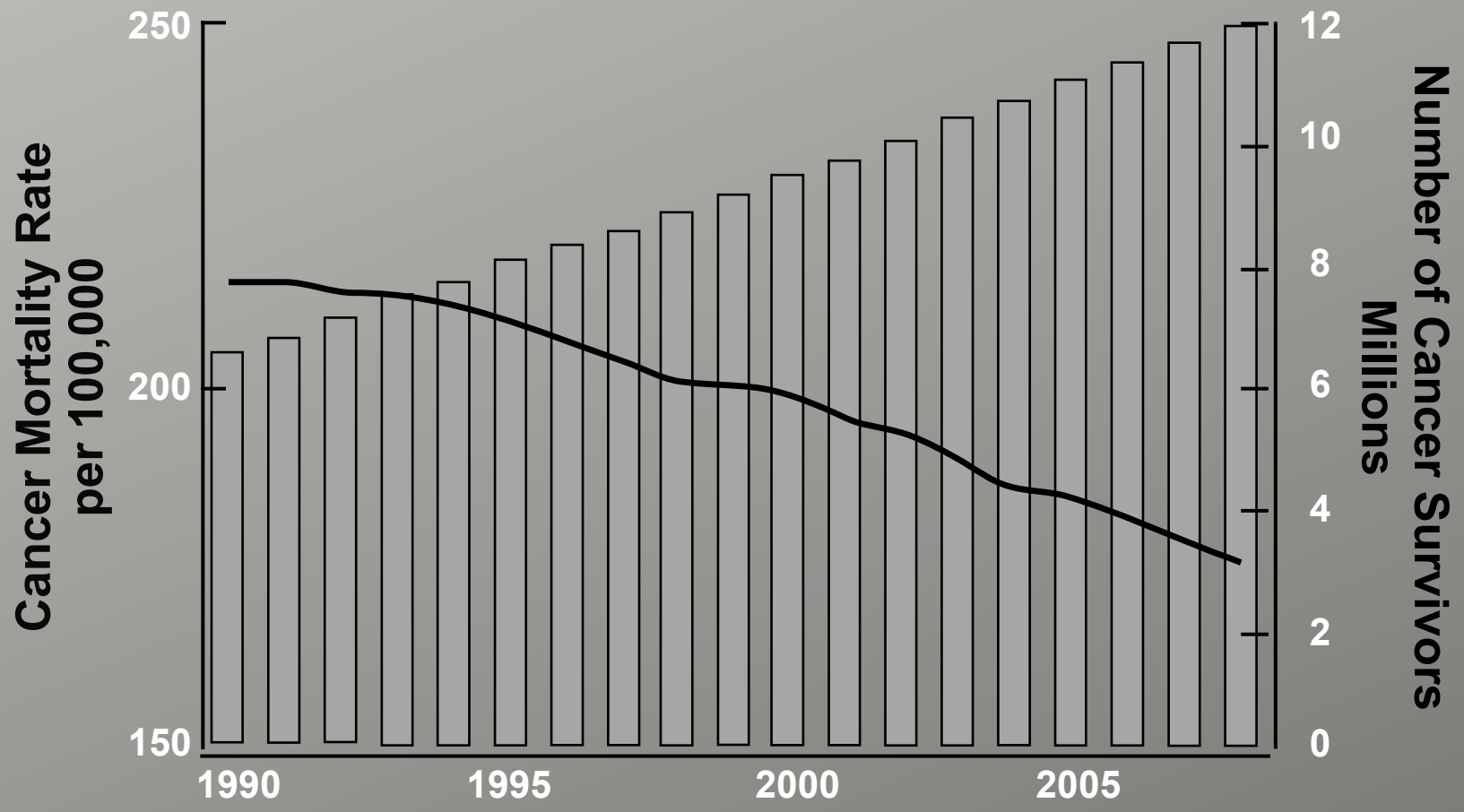


Patologia Cardioncologica

Monica Baroni
Fondazione Toscana
"G.Monasterio"

Di tumore non si muore….necessariamente

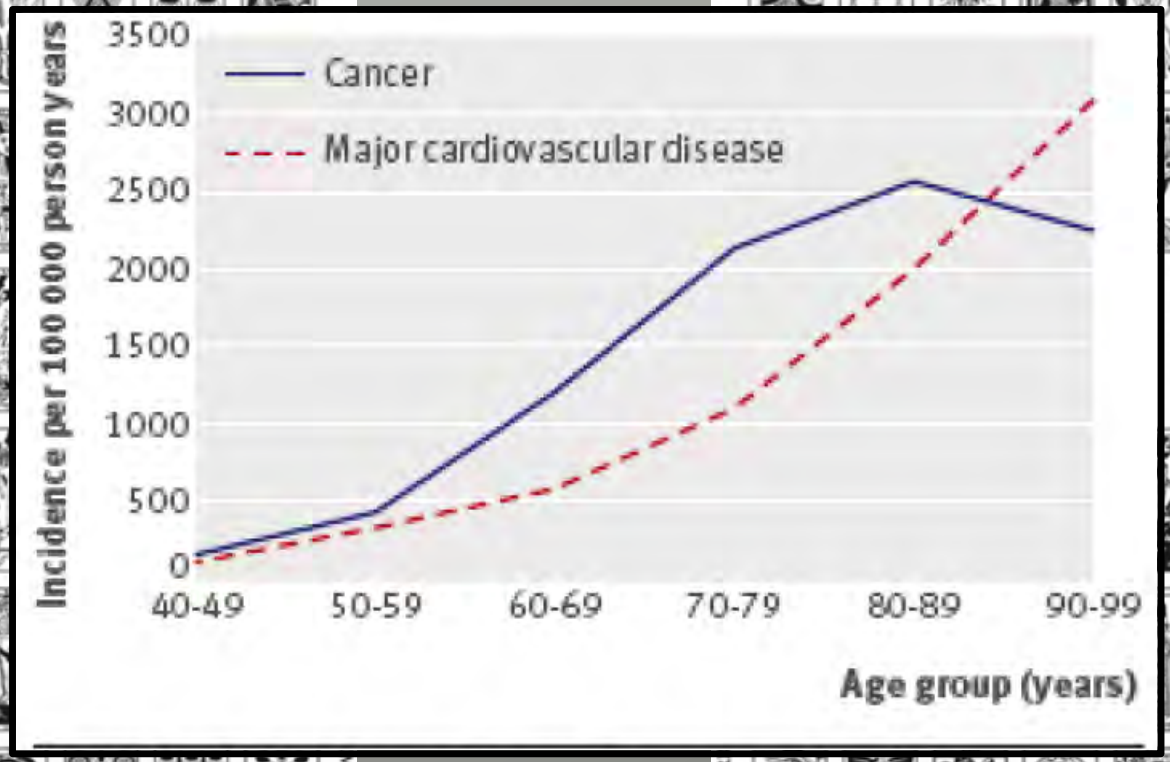


Stima della sopravvivenza e della mortalità "age-adjusted" per tumore/100.000 persone in U.S.A
Dati del National Cancer Institute

Cancro e Malattie Cardiovascolari

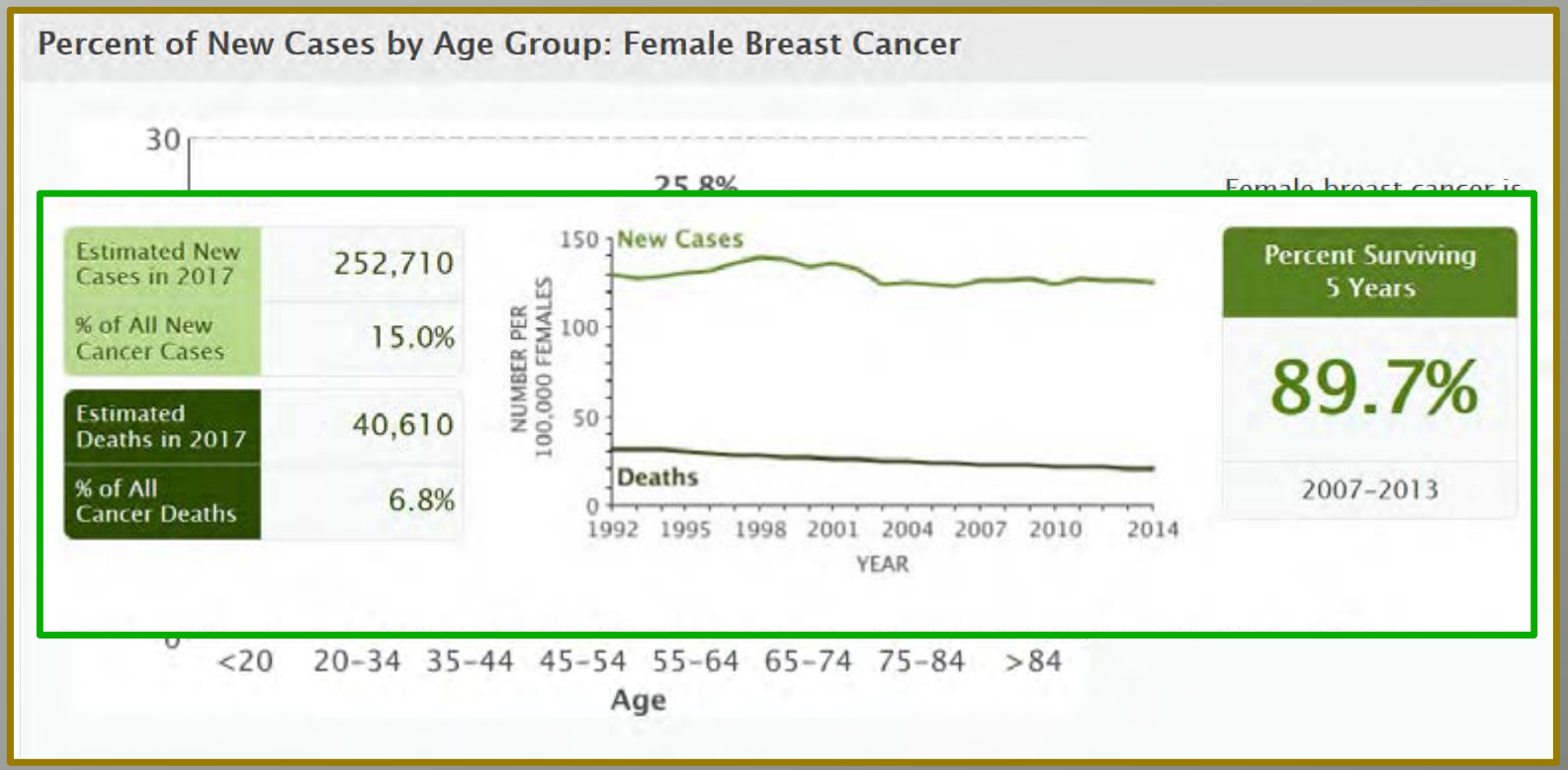
Storia di Destini Incrociati…

In ogni paziente c'è alta probabilità che la malattia tumorale e quella cardiovascolare si sovrappongono



Cancro e Malattie Cardiovascolari

E' un problema di genere?



- *Ogni anno ci sono circa 125 nuovi casi di tumore alla mammella su 100.000 donne*
- *Mortalità annua aggiustata per età 21 casi/100.000*
- *Circa 12.4% della popolazione femminile avrà una diagnosi di tumore alla mammella durante la vita*

Mortalità nelle donne sopravvissute a Tumore Mammario

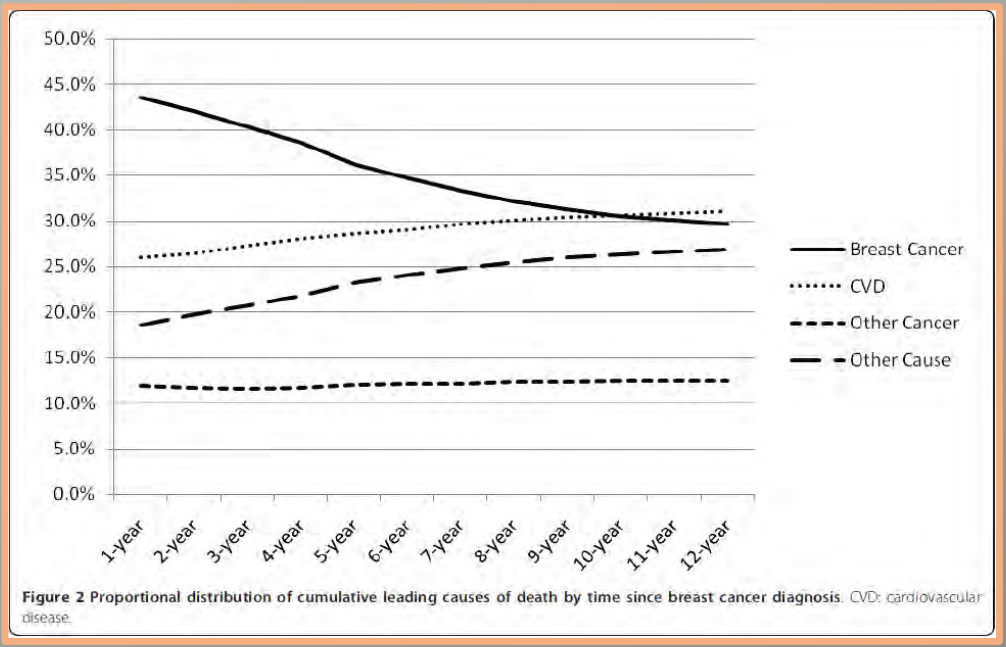


Figure 2 Proportional distribution of cumulative leading causes of death by time since breast cancer diagnosis. CVD: cardiovascular disease.

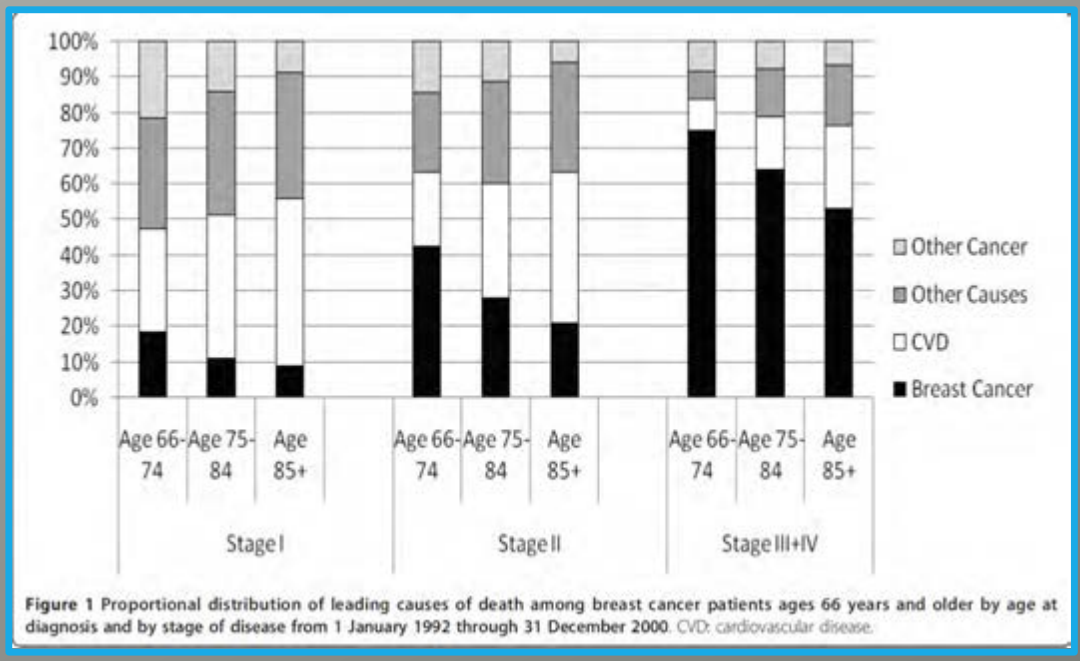
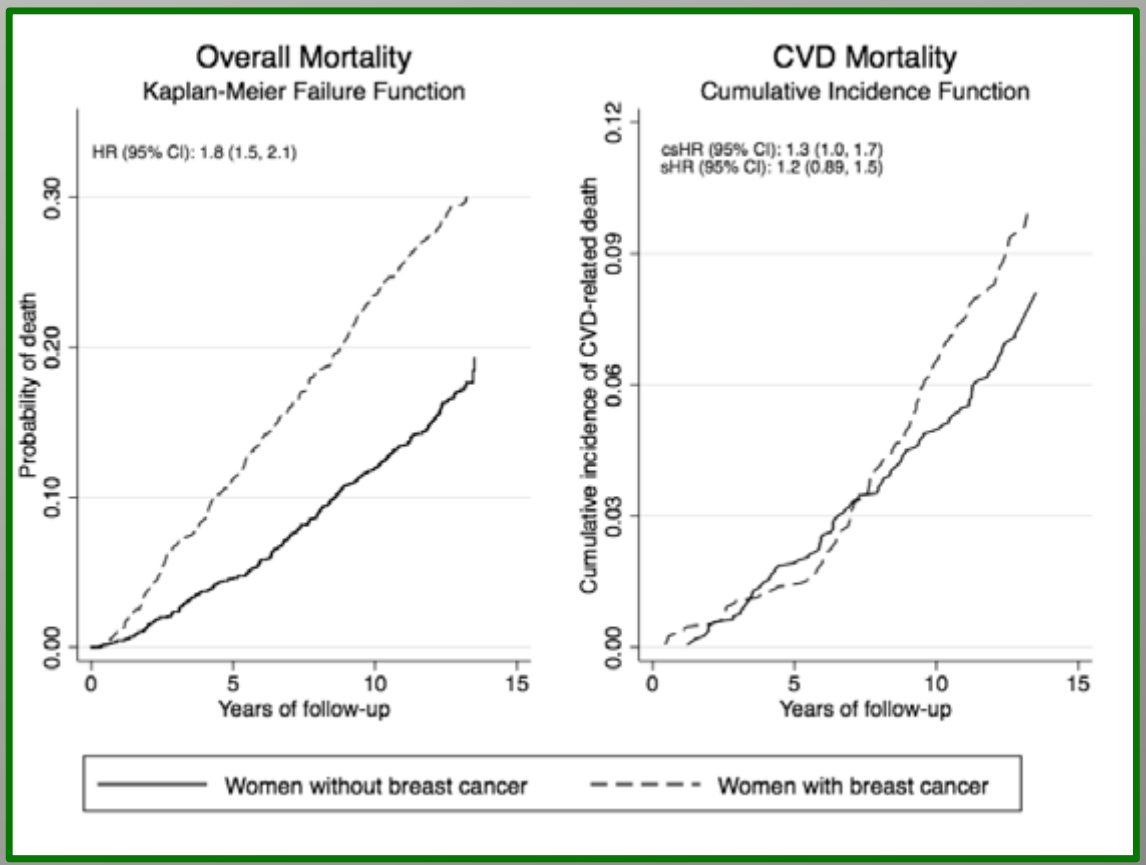


Figure 1 Proportional distribution of leading causes of death among breast cancer patients ages 66 years and older by age at diagnosis and by stage of disease from 1 January 1992 through 31 December 2000. CVD: cardiovascular disease.

Patnaik JL, et al. Cardiovascular disease competes with breast cancer as leading cause of death for older female diagnosed with breast cancer.. Breast Cancer Research 2011

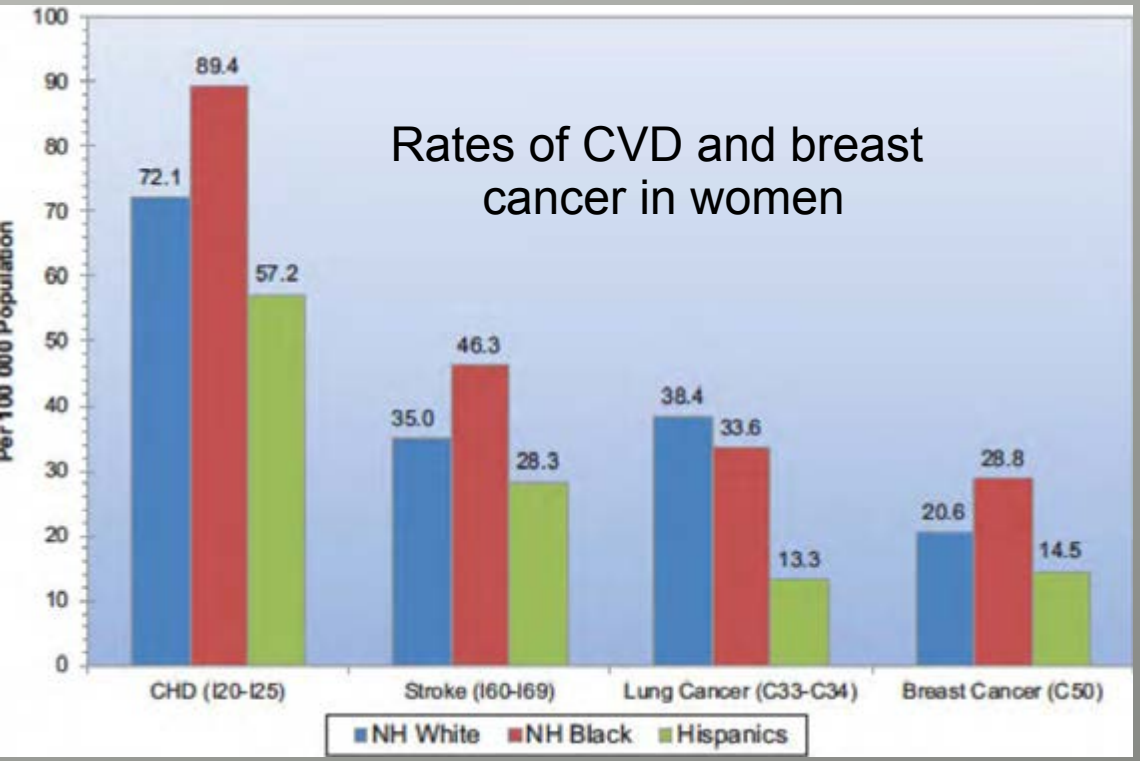
Mortalità Cardiovascolare nel Tumore Mammario



Time since beginning of follow-up	Overall Mortality HR[a] (95% CI) Women without Breast Cancer (235 deaths)	Breast Cancer Survivors (407 deaths)	p[b]
0-6 years	1.0	2.2 (1.7, 2.8)	0.04
>6 years	1.0	1.5 (1.3, 1.9)	
Time since beginning of follow-up	**CVD Mortality Women without Breast Cancer (114 deaths)**	**Breast Cancer Survivors (155 deaths)**	
	Cause-specific HR[a,c] (95% CI)		*p*[b]
0-7 years	1.0	0.80 (0.53, 1.2)	0.004
>7 years	1.0	1.8 (1.3, 2.5)	
	Subdistribution HR[a,d] (95% CI)		p[b]
0-7 years	1.0	0.59 (0.40, 0.87)	<0.001
>7 years	1.0	1.9 (1.4, 2.7)	

Bradshaw P., et al. Cardiovascular Disease Mortality Among Breast Cancers Survivors. Epidemiology 2016

Mortalità per Cancro alla mammella e Mortalittà Cardiovascolare



Conclusioni Studio Women's Health Initiative (prospettico 100000 donne)

CVD risulta la principale causa di morte a 10 anni nelle donne con tumore localizzato nella fascia di età 70-79 anni

Mortalità per tumore mammario 17% vs mortalità CVD 22%

Rispetto alle coetanee che non hanno avuto tumore della mammella hanno lo stesso rischio di cardiopatia ischemica ma con minore numero di fattori di rischio cardiovascolare e con più alta mortalità

Heart Disease and Stroke Statistics—2017 Update

A Report From the American Heart Association *Circulation.* 2017 March 07

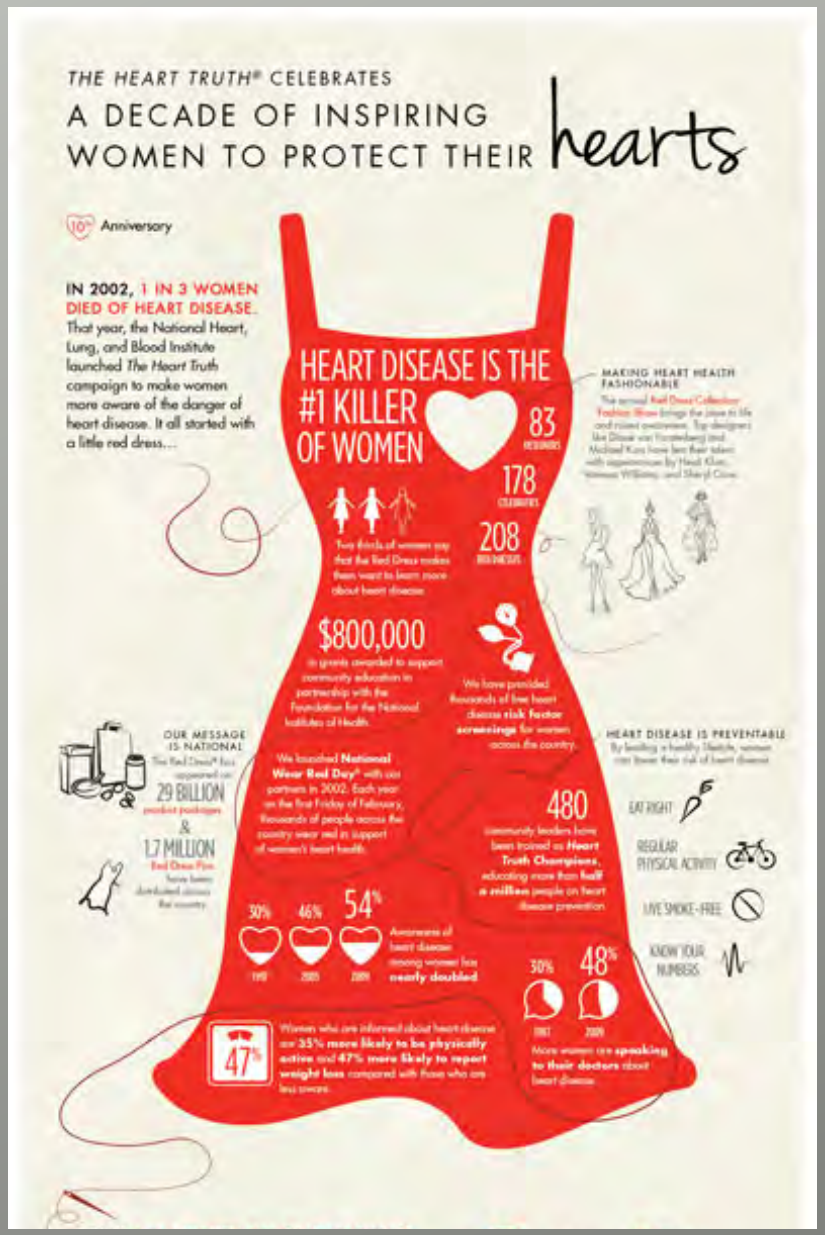
RESEARCH ARTICLE

Cardiovascular disease and mortality after breast cancer in postmenopausal women: Results from the Women's Health Initiative

Na-Jin Park[1*], Yuefang Chang[2], Catherine Bender[1], Yvette Conley[1], Rowan T. Chlebowski[3], G. J. van Londen[4], Randi Foraker[5], Sylvia Wassertheil-Smoller[6], Marcia L. Stefanick[7], Lewis H. Kuller[8]

PLOS ONE | https://doi.org/10.1371/journal.pone.0184174 September 21, 2017

Mortalità Femminile



1 morte su 3.3 attribuibile a CVD

1 morte su 8.3 a CHD

1 morte su 31.5 attribuibile a cancro della mammella

Dati Center Disease Control and Prevention 2014

Mehta et al. Circulation 2018

Una nuova (??) disciplina
CARDIONCOLOGIA

MAYO CLINIC

REVIEW

Evaluation and Management of Patients With

Hear

Joerg He

Hector F

EUROPEAN SOCIETY OF CARDIOLOGY®

European Heart Journal – Cardiovascular Imaging (2014) **15**, 1063–1093
doi:10.1093/ehjci/jeu192

POSITION PAPER

DOCUMENTO DI CONSENSO

Documento di consenso ANMCO/AICO/AIOM: Snodi clinico-gestionali in ambito cardioncologico

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)

Una nuova (??) disciplina
CARDIONCOLOGIA

Cardiologia. 1996 Sep;41(9):887-91.

[A new frontier: cardio-oncology]

[Article in Italian]

Cardinale D.

Servizio di Cardiologia, Istituto Europeo di Oncologia, IRCCS, Milano.

PMID: 8983846 [PubMed - indexed for MEDLINE]

MeSH Terms, Substances

Current Cardiology Reports

June 2016, 18:51 | Cite as

Curing Cancer, Saving the Heart: A Challenge That Cardioncology Should Not Miss

Authors | Authors and affiliations

Daniela Cardinale, Gina Biasillo, Carlo Maria Cipolla

Ruolo della Cardioncologia

- *Fornire definizioni uniformi e condivise della cardiotossicità*
- *Identificare percorsi di diagnosi e trattamento del paziente oncologico prima, durante e dopo la terapia antitumorale*
- *Proporre modelli organizzativi efficienti e sostenibili*

AHA SCIENTIFIC STATEMENT

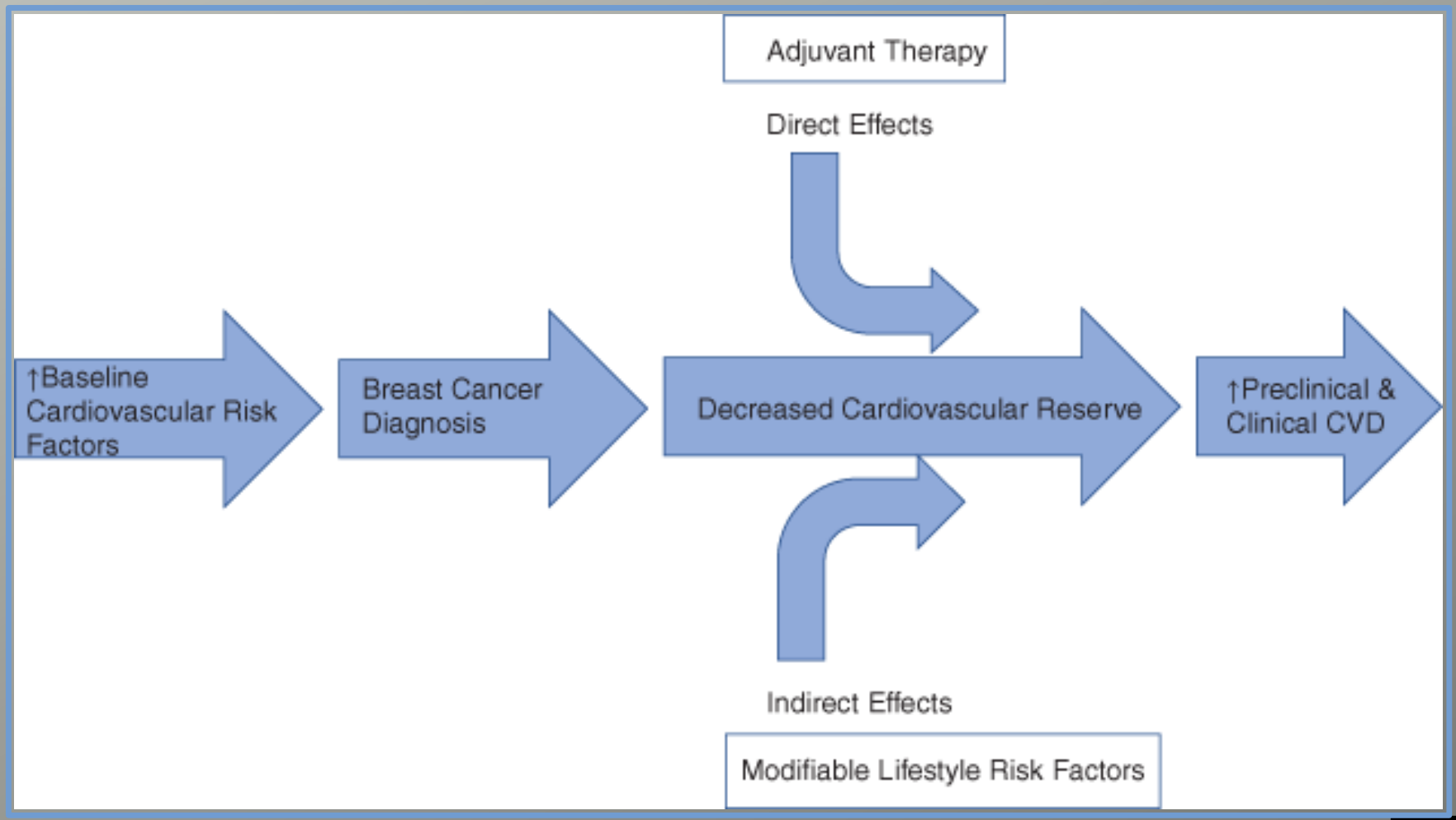
Cardiovascular Disease and Breast Cancer: Where These Entities Intersect

A Scientific Statement From the American Heart Association

Mehta L.S, et al Circulation 2018

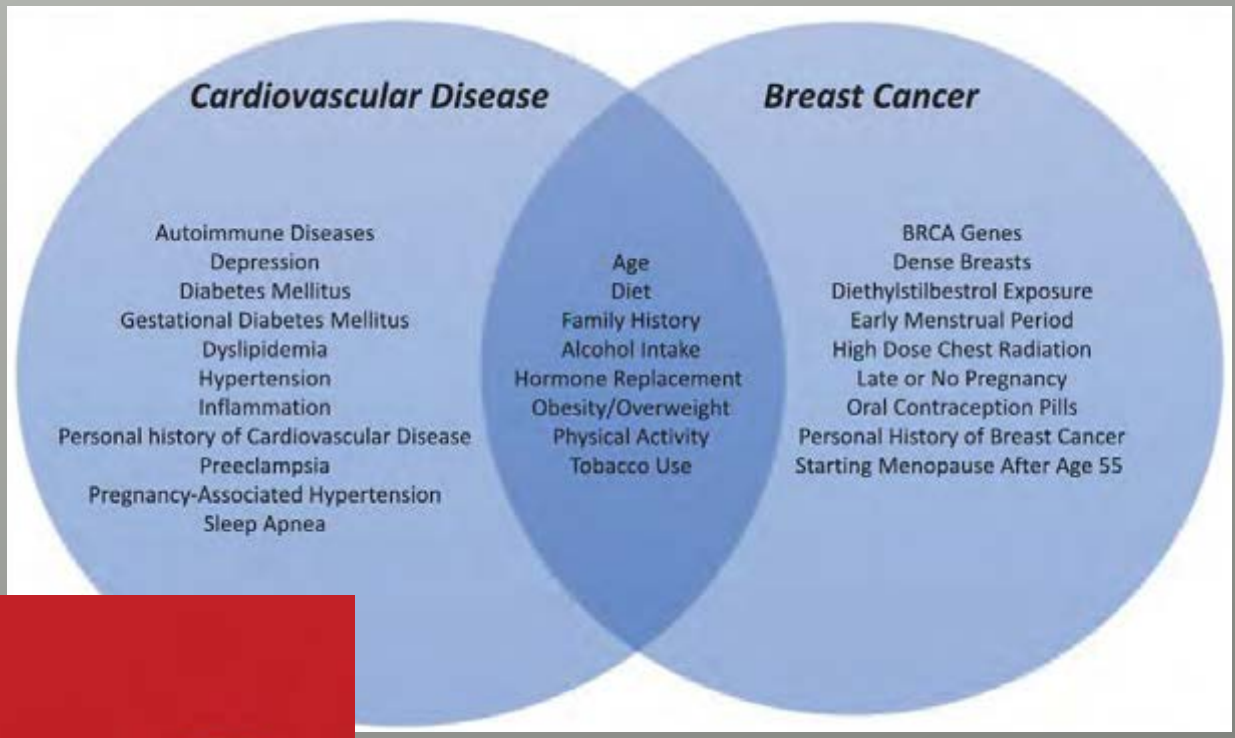
Tumore mammario e malattie cardiovascolari

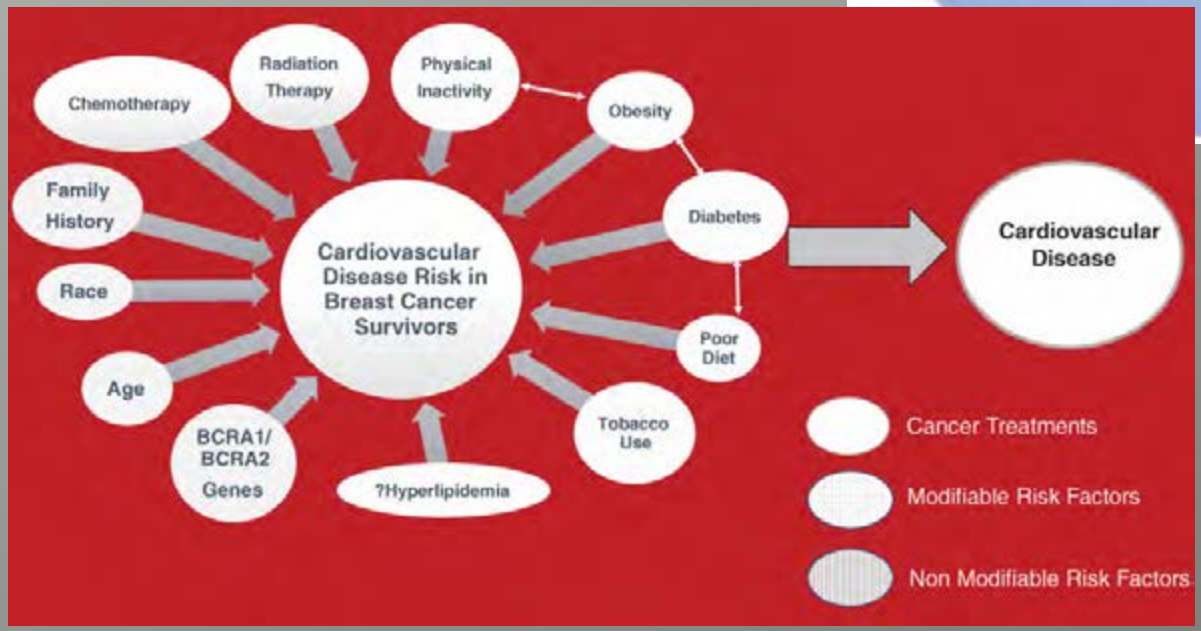
The multiple-hit hypotesis



Clinical Cardiology
15 FEB 2018 DOI: 10.1002/clc.22886

Malattie cardiovascolarie tumore alla mammella
A tight connection





Clinical Cardiology
15 FEB 2018 DOI: 10.1002/clc.22886

Fattori di Rischio per cardiopatia e tumore mammario

	Risk of CVD	Risk of Breast Cancer
Healthy Diet	↓	↓
Western Diet	↑	↑
Light-Moderate Alcohol Intake	↓	↑
Red/Processed Meat	↑	↑
Physical Activity	↓	↓
Sedentary Lifestyle	↑	↑
Premenopausal Obesity	↑	↓
Smoking	↑	↑
Early Menarche	↑	↑
Early Menopause	↑	↓
Hormone Replacement Therapy	↑	↑

Complicanze Cardiovascolari nel Percorso Oncologico

- *Disfunzione ventricolare e scompenso*
- *Patologia Coronarica*
- Patologia Valvolare
- Aritmie
- Ipertensione arteriosa
- Patologia Tromboembolica
- Patologia vascolare periferica e stroke
- Ipertensione polmonare
- Complicanze pleuropericardiche

2016 ESC Position Paper on cancer treatments and cardiovascular toxicity

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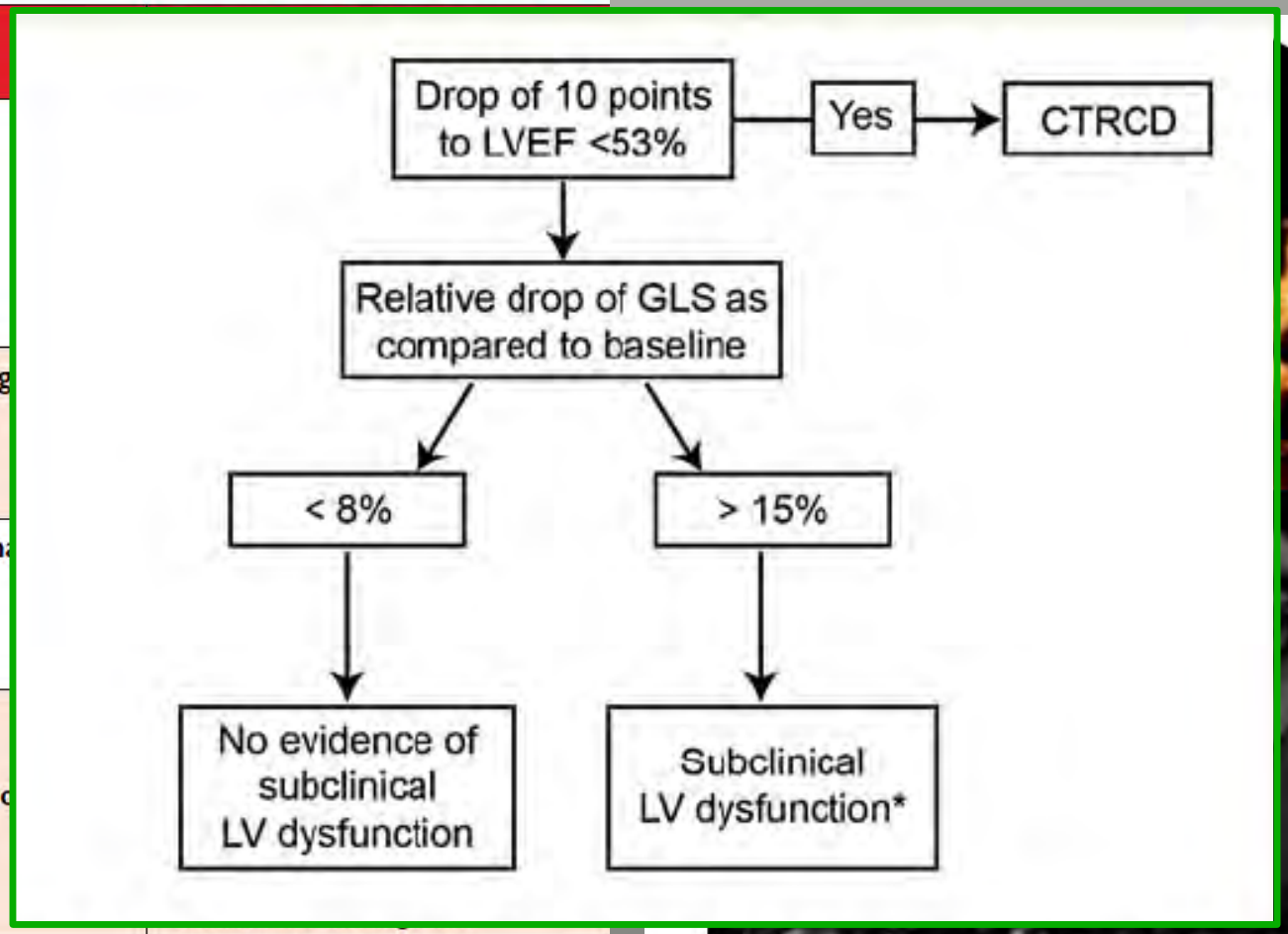
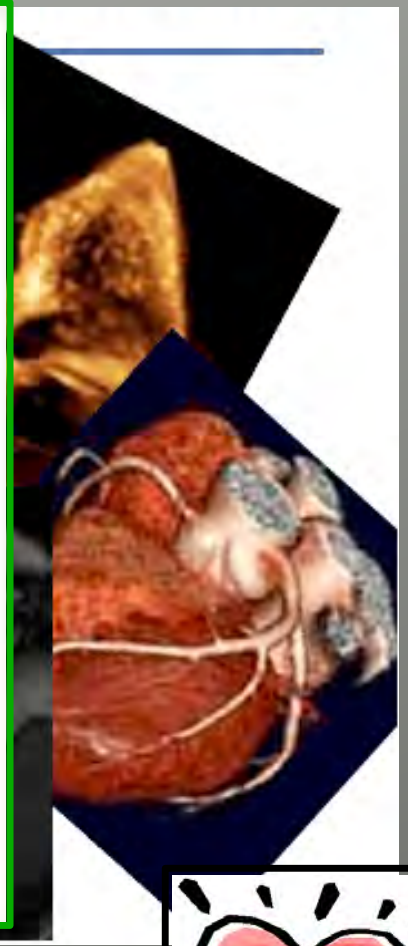
2016 ESC Position Paper on cancer treatments and cardiovascular toxicity

Chemiotherapy-Related Cardiac Dysfunction (CTRCD)

Technique
Echocardiography: - 3D-based LVEF - 2D Simpson's LVEF - GLS
Nuclear cardiac imaging (MUGA)
Cardiac magnetic reson
Cardiac biomarkers: - Troponin I - High-sensitivity Tropo - BNP - NT-proBNP





2016 ESC Position Paper on cancer treatments and cardiovascular toxicity

Regimi terapeutici associati a CTRCD tipo I e II

Cancer

	Tipo I	Tipo II
Agenti responsabili	Doxorubicina	Trastuzumab
Tipo di decorso e risposta alla terapia cardioprotettrice	Il danno è permanente e irreversibile. C'è possibilità di stabilizzazione, ma può recidivare anche a distanza di anni	Con l'interruzione del trattamento possibilità di recupero
Dose-effetto	Dose effetto-correlata e cumulativa	Non dose effetto-correlata
Rechallenge	Alta probabilità di una disfunzione ricorrente, progressiva, che può esitare in un intrattabile scompenso cardiaco e morte	Sono necessari dati maggiori per poter valutare la possibilità di rechallenge
Danni ultrastrutturali	Vacuolizzazione, disarrangiamenti e dispersione delle miofibrille; necrosi	Non apparenti danni ultrastrutturali

- Bevacizumab
- Bortezomib

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Fattori di rischio per CTRCD tipo I

Risk factors

- Cumulative dose
- Female sex
- Age
  - >65 years old
  - Paediatric population (<18 years)
- Renal failure
- Concomitant or previous radiation therapy involving the heart
- Concomitant chemotherapy
  - alkylating or antimicrotubule agents
  - immuno- and targeted therapies
- Pre-existing conditions
  - Cardiac diseases associating increased wall stress
  - Arterial hypertension
  - Genetic factors

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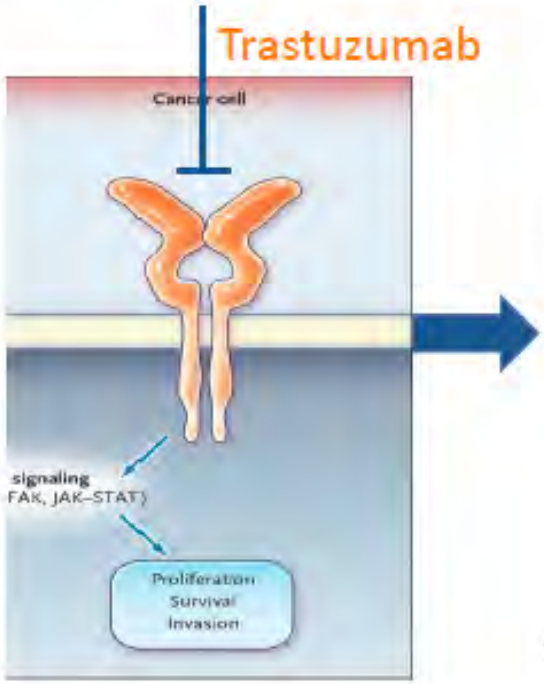
Trastuzumab improves survival in metastatic HER2-positive breast cancer



Slamon et al. NEJM. 2001;344:783

Tumori che esprimono recettori ormonali per estrogeni e/o progesterone

Tumori con iperespressione human epidernal growth factor receptor 2 (HER2+)

Tumori che non esprimono i recettori ormonali per gli estrogeni e per il progesterone ed il recettore HER2 (tumori triplo negativi)

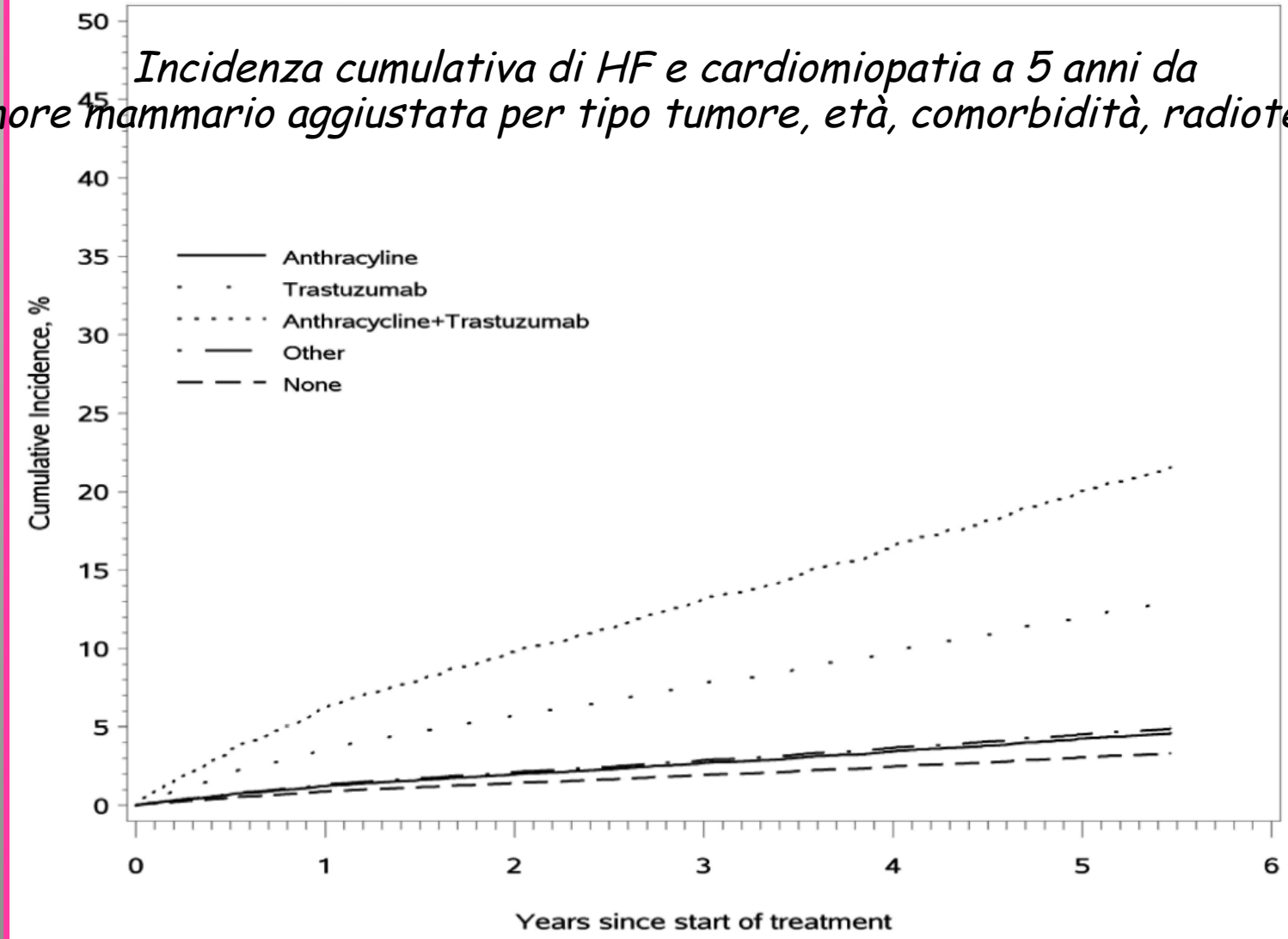
Fattori di Rischio per CRTCD tipo II

- Age, female sex, postmenopausal status
- Genetic factors
  - Functional polymporphisms of genes involved in anthracycline pathways?
  - HER2 gene ?
  - BRCA mutation?
- CV risk factors and CV disease
  - Hypertension, diabetes, smoking
  - CAD, prior LV dysfunction or heart failure

Chemiotherapy-Related Cardiac Dysfunction (CTRCD)

Rischio Cumulativo

Incidenza cumulativa di HF e cardiomiopatia a 5 anni da tumore mammario aggiustata per tipo tumore, età, comorbidità, radioterapia

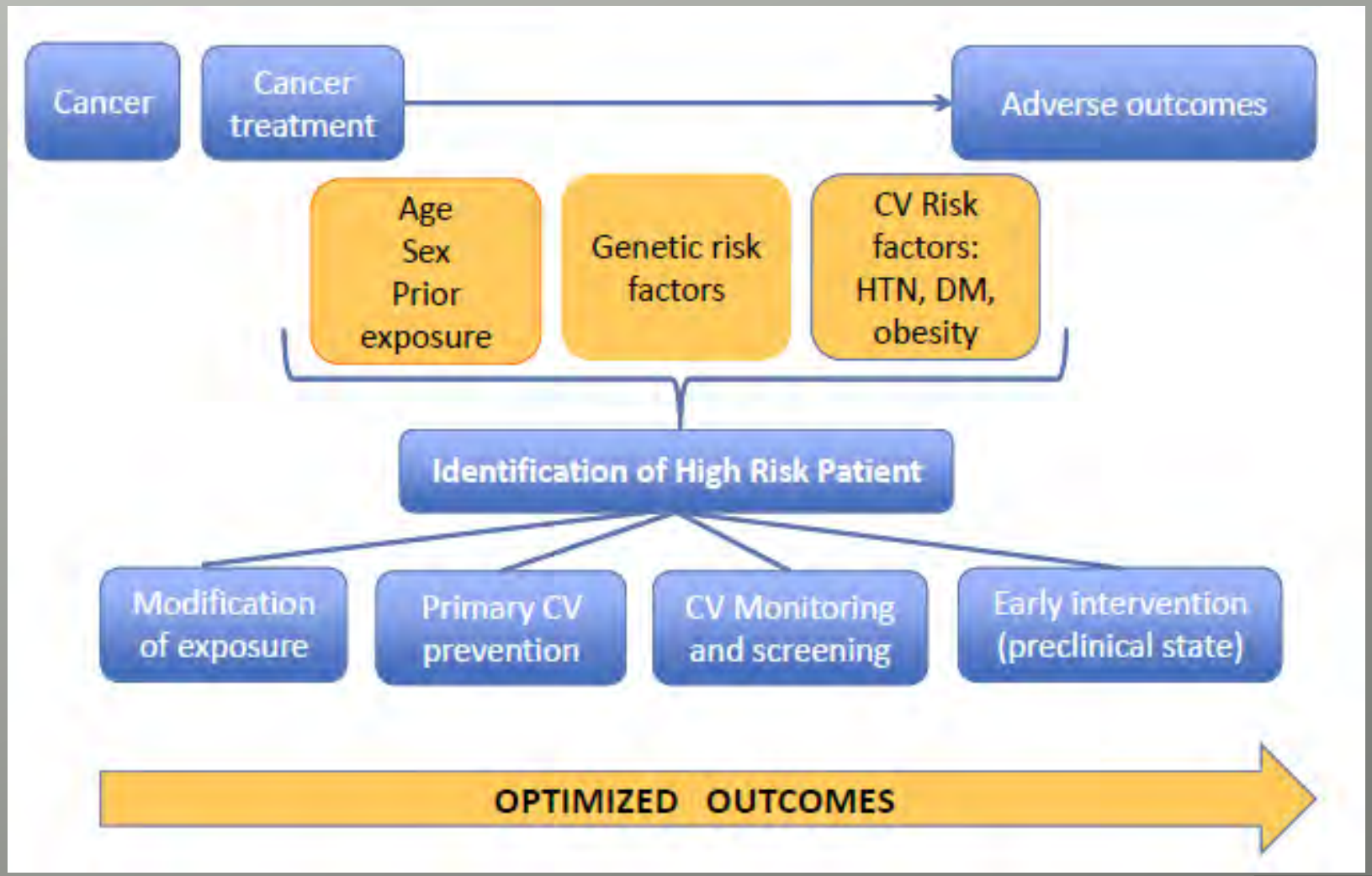


Risk of Heart Failure in Breast Cancer Patients After Anthracycline and Trastuzumab Treatment: A Retrospective Cohort Study

Erin J. Aiello Bowles, Robert Wellman, Heather Spencer Feigelson, Adedayo A. Onitilo, Andrew N. Freedman, Thomas Delate, Larry A. Allen, Larissa Nekhlyudov, Katrina A. B. Goddard, Robert L. Davis, Laurel A. Habel, Marianne Ulcickas Yood, Catherine McCarty, David J. Magid, Edward H. Wagner; for the Pharmacovigilance Study Team

Manuscript received January 05, 2012; revised June 13, 2012; accepted June 18, 2012.

Stratificazione del Rischio per CRTCD



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Complicanze Cardiovascolari nel Percorso Oncologico

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- *Ipertensione polmonare*
- *Complicanze pleuropericardiche*

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Complicanze Ischemiche nel Percorso Oncologico

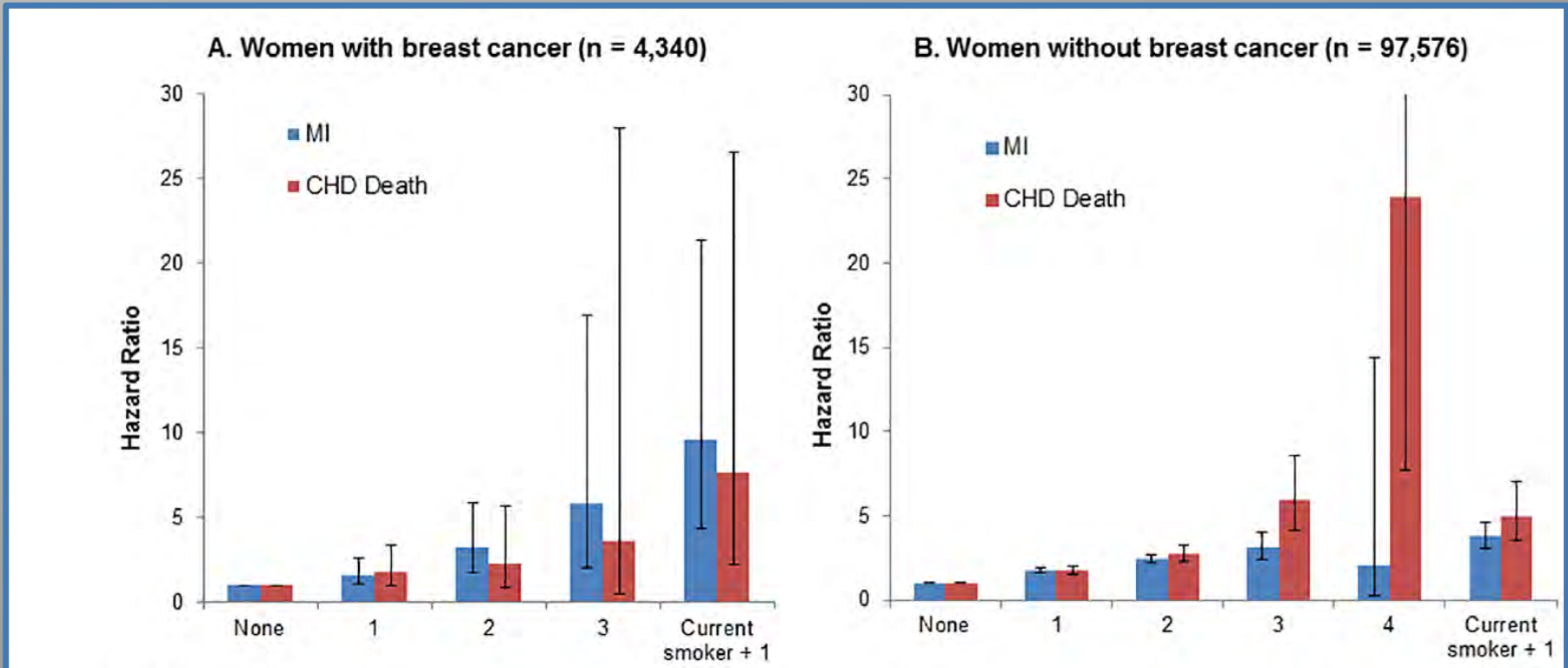


Fig 4. Hazard ratios of myocardial infarction (MI) and coronary heart disease (CHD)-related death by the number of baseline risk factors (i.e., smoking, hypertension, hypercholesterolemia, and diabetes) in women with (A) and without (B) breast cancer [a]. [a]Cox

RESEARCH ARTICLE

Cardiovascular disease and mortality after breast cancer in postmenopausal women: Results from the Women's Health Initiative

Na-Jin Park[1]*, Yuefang Chang[2]*, Catherine Bender[1], Yvette Conley[1], Rowan T. Chlebowski[3], G. J. van Londen[4], Randi Foraker[5], Sylvia Wassertheil-Smoller[6], Marcia L. Stefanick[7], Lewis H. Kuller[8]*

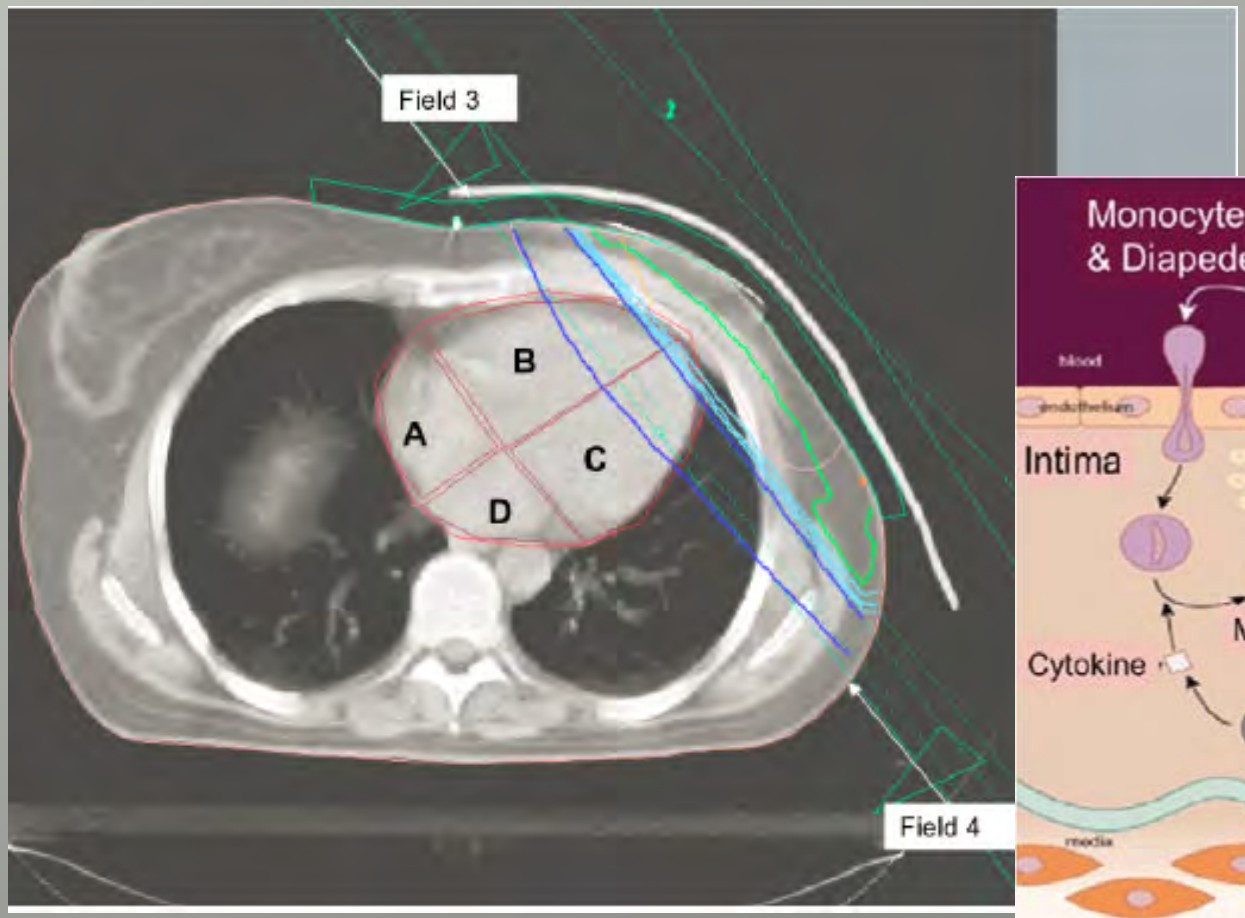
PLOS ONE | https://doi.org/10.1371/journal.pone.0184174 September 21, 2017

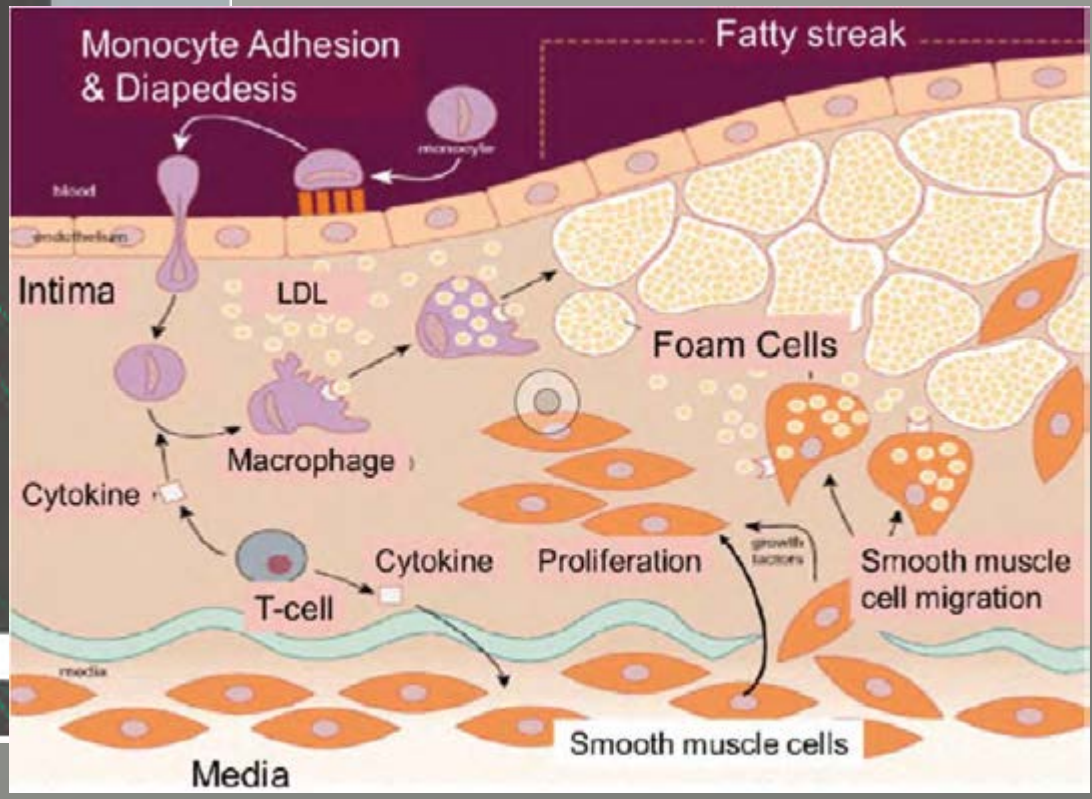
Complicanze Ischemiche nel Percorso Oncologico

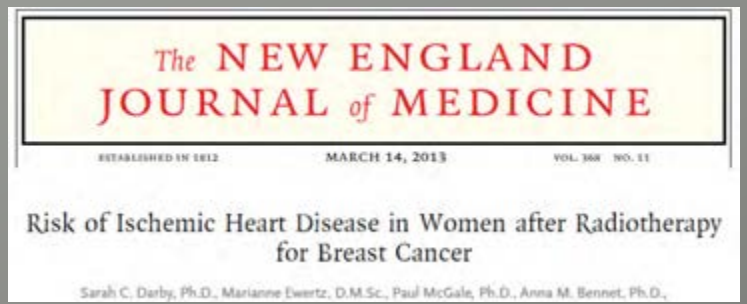
Agent	Pathophysiological mechanism	Risk of coronary artery disease and acute coronary syndrome
Fluoropyrimidines (5-FU, capecitabine, gemcitabine)	• Endothelial injury • Vasospasm	• Up to 18% manifest myocardial ischaemia • Up to 7–10%: silent myocardial ischaemia
Platinum compounds (cisplatin)	• Procoagulant status • Arterial thrombosis	• 20-year absolute risk of up to 8% after testicular cancer • 2% risk of arterial thrombosis
VEGF inhibitors (bevacizumab, sorafenib, sunitinib)	• Procoagulant status • Arterial thrombosis • Endothelial injury	• Risk of arterial thrombosis: bevacizumab 3.8%, sorafenib 1.7%, sunitinib 1.4%

2016 ESC Position Paper on cancer treatments and cardiovascular toxicity

Effetti Cardiovascolari della Radioterapia






The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 14, 2013 VOL. 368 NO. 11

Risk of Ischemic Heart Disease in Women after Radiotherapy for Breast Cancer

Sarah C. Darby, Ph.D., Marianne Ewertz, D.M.Sc., Paul McGale, Ph.D., Anna M. Bennet, Ph.D.,

Eventi Cardiovascolari e Radioterapia

Years from breast cancer diagnosis to cardiac death	No radiotherapy: Cardiac deaths left/right	No radiotherapy: Cardiac mortality ratio, left-sided vs right-sided (95% CI)	Radiotherapy: Cardiac deaths left/right	Radiotherapy: Cardiac mortality ratio, left-sided vs right-sided (95% CI)
Diagnosed 1973–82				
<5 years	717/679	0·98 (0·89–1·09)	230/180	1·19 (0·98–1·45)
5–9	673/614	1·04 (0·93–1·15)	189/145	1·21 (0·97–1·50)
10–14	469/441	1·00 (0·87–1·13)	157/106	1·42 (1·11–1·82)
⩾15	515/480	1·01 (0·89–1·15)	234/145	1·58 (1·29–1·95)
Diagnosed 1983–92				
<5 years	880/785	1·06 (0·96–1·16)	245/227	1·00 (0·84–1·20)
5–9	815/729	1·07 (0·97–1·18)	249/218	1·08 (0·90–1·29)
⩾10	390/361	1·04 (0·90–1·20)	144/108	1·27 (0·99–1·63)
Diagnosed 1993–2001				
<5 years	567/508	1·05 (0·93–1·18)	225/226	0·95 (0·79–1·14)
5–9	144/136	1·02 (0·81–1·29)	83/79	0·99 (0·73–1·35)

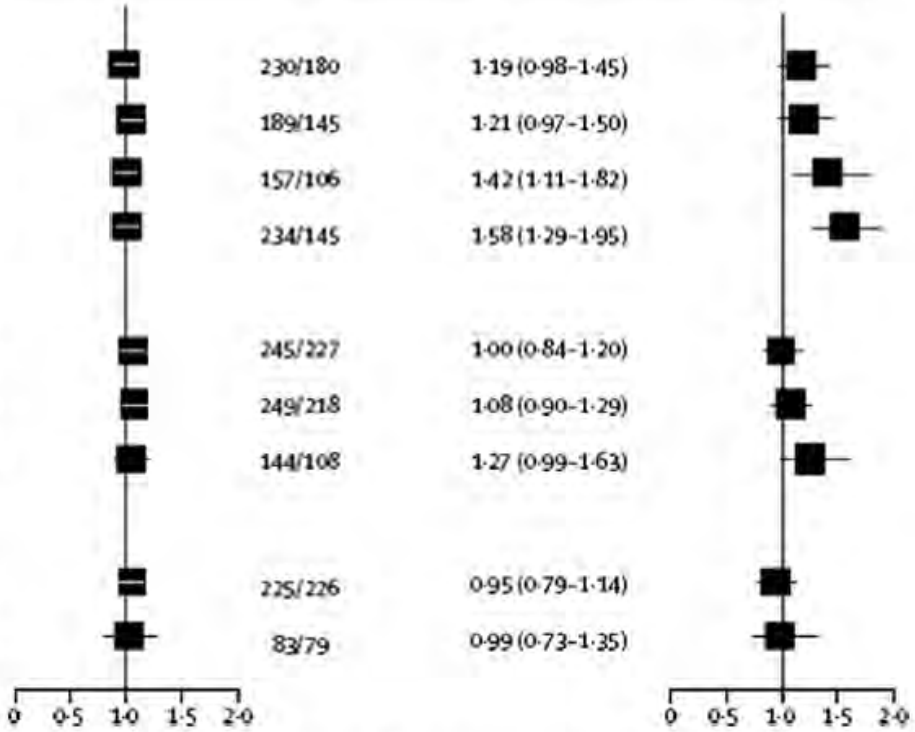


Fig. 1. Left-side vs. right-side breast cancer RT: subsequent cardiac mortality ratios by years from breast cancer diagnosis to cardiac death shared out into period of diagnosis and radiotherapy status (by Darby et al. [32], with permission from Elseiver).

Radiation-induced cardiac damage in early left breast cancer patients: Risk factors, biological mechanisms, radiobiology, and dosimetric constraints

Radiotherapy and Oncology 103 (2012) 133–142

Angela Sardaro [a], Maria Fonte Petruzzelli [b], Maria Patrizia D'Errico [c], Luca Grimaldi [d], Giorgio Pili [d],

Eventi Cardiovascolari e Radioterapia

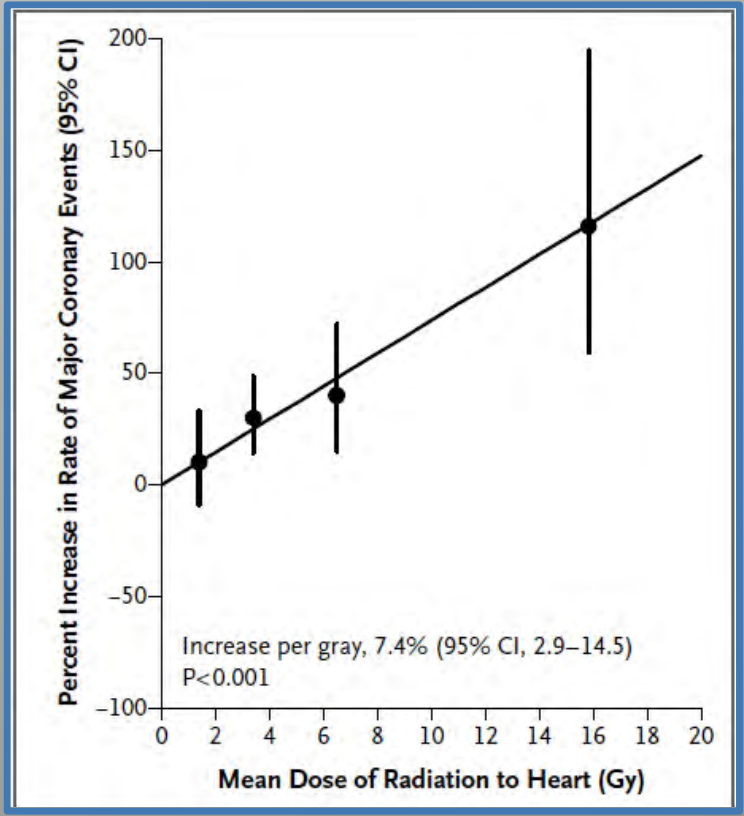
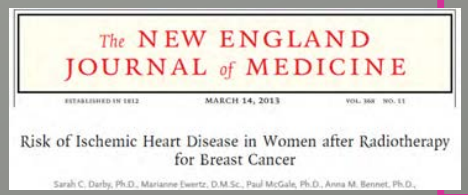


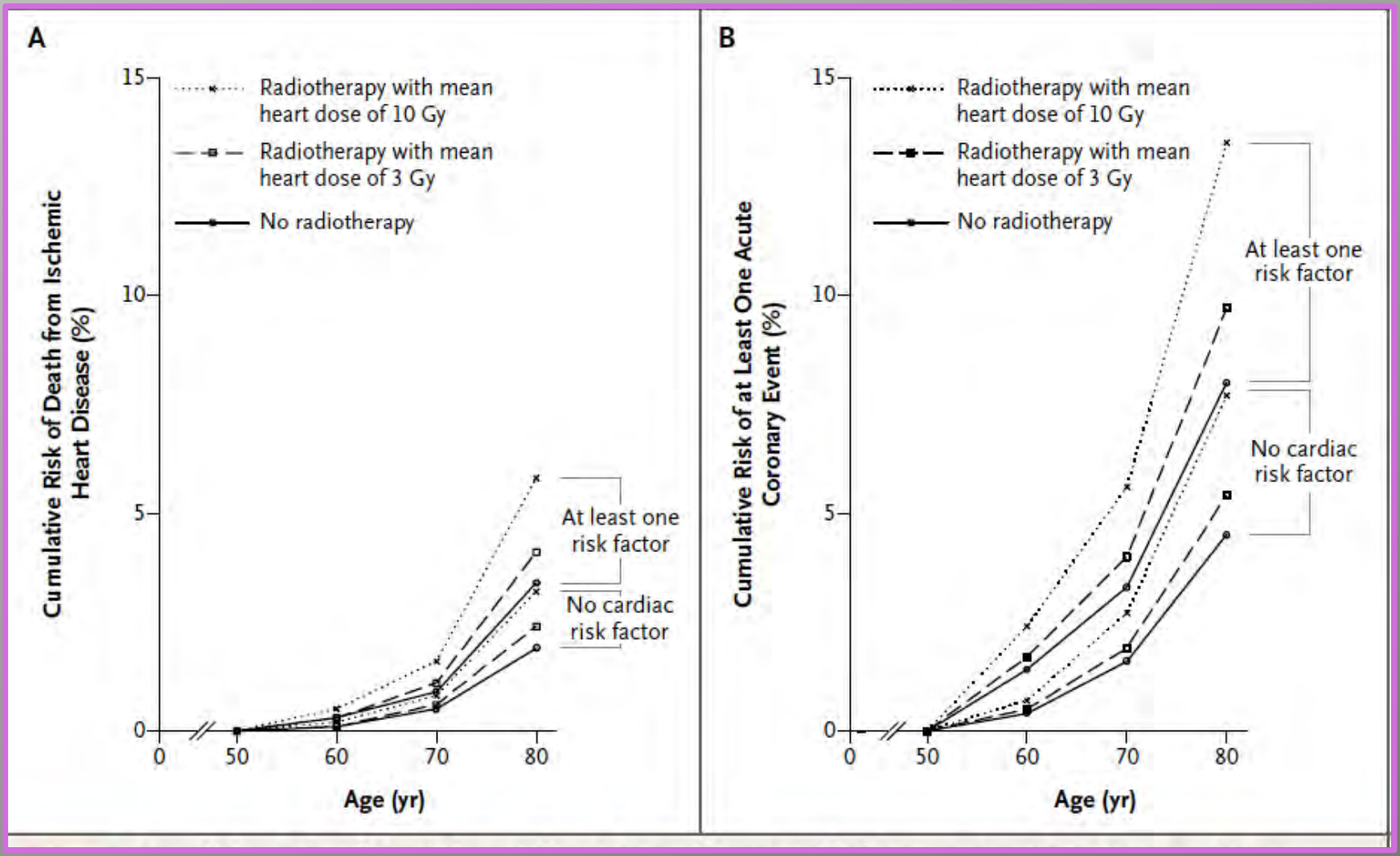
Table 3. Percentage Increase in the Rate of Major Coronary Events per Gray, According to Time since Radiotherapy.

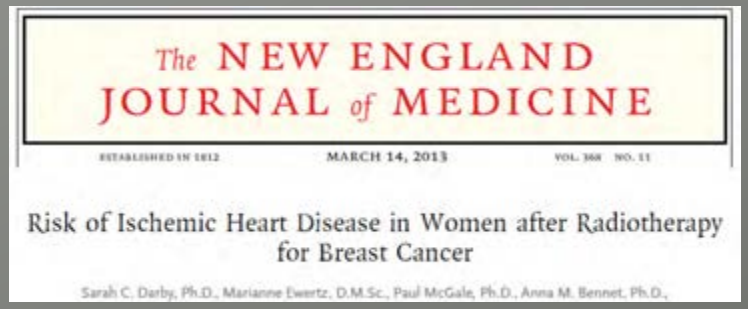
Time since Radiotherapy*	No. of Case Patients	No. of Controls	Increase in Rate of Major Coronary Events (95% CI)†
			% increase/Gy
0 to 4 yr	206	328	16.3 (3.0 to 64.3)
5 to 9 yr	216	296	15.5 (2.5 to 63.3)
10 to 19 yr	323	388	1.2 (−2.2 to 8.5)
≥20 yr	218	193	8.2 (0.4 to 26.6)
0 to ≥20 yr	963	1205	7.4 (2.9 to 14.5)

Indipendentemente dai fattori CVD al momento della radioterapia
Il rischio di eventi coronarici maggiori
aumenta in modo lineare con la dose
cui viene esposto il cuore, senza apparente soglia
L'aumento del rischio avviene dopo 5° anno e si mantiene
nella 3 decade dopo radioterapia



Eventi Cardiovascolari e Radioterapia

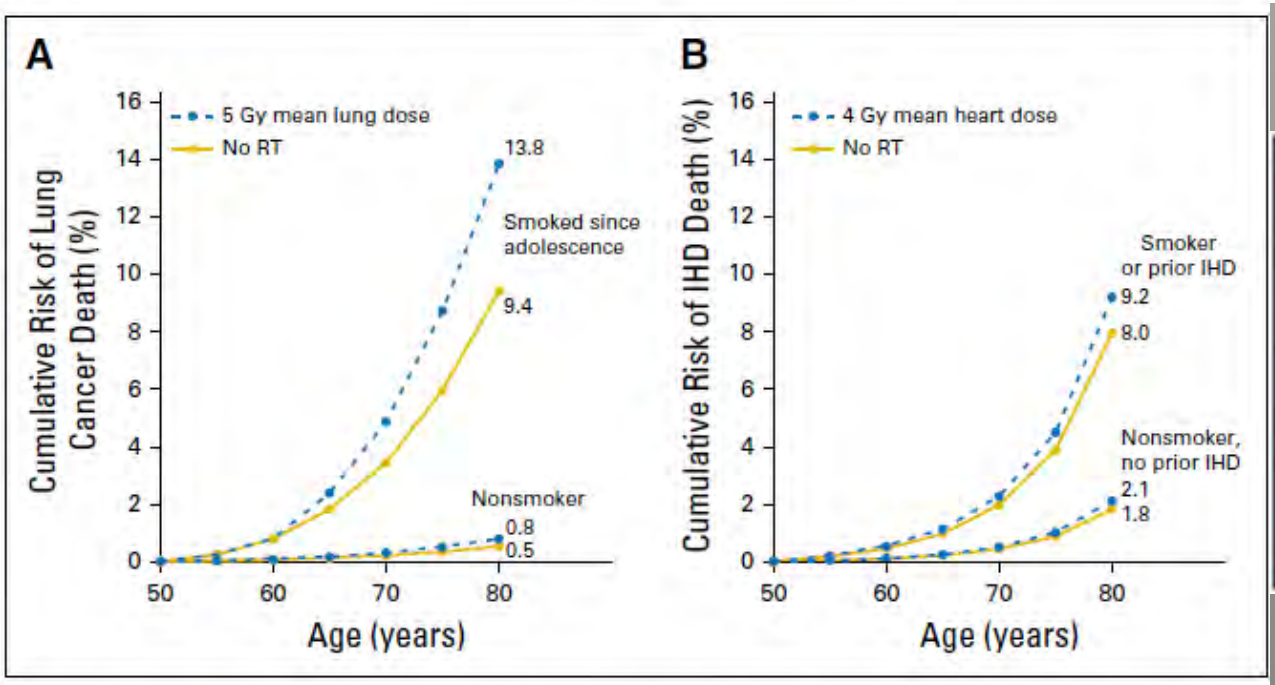




Eventi Cardiovascolari e Radioterapia

Rapporto costo/beneficio

For long-term smokers, the absolute risks of modern radiotherapy may outweigh the benefits, yet for most nonsmokers (and ex-smokers), the benefits of radiotherapy far outweigh the risks. Hence, smoking can determine the net effect of radiotherapy on mortality, but smoking cessation substantially reduces radiotherapy risk.



VOLUME 35 · NUMBER 15 · MAY 20, 2017
JOURNAL OF CLINICAL ONCOLOGY
ORIGINAL REPORT

Estimating the Risks of Breast Cancer Radiotherapy: Evidence From Modern Radiation Doses to the Lungs and Heart and From Previous Randomized Trials

Carolyn Taylor, Candace Correa, Frances K. Duane, Marianne C. Aznar, Stewart J. Anderson, Jonas Bergh,

Eventi Cardiovascolari e Radioterapia

Risk factors for radiation-induced heart disease

Anterior or left chest irradiation location

High cumulative dose of radiation (> 30 Gy)

Younger age (< 50) at time of radiation therapy

High dose of radiation fractions (> 2 Gy/day)

Presence and extent of tumor in or next to the heart

Inadequate or absent shielding

Concomitant chemotherapy (eg, anthracyclines)

Cardiovascular risk factors

Preexisting cardiovascular disease

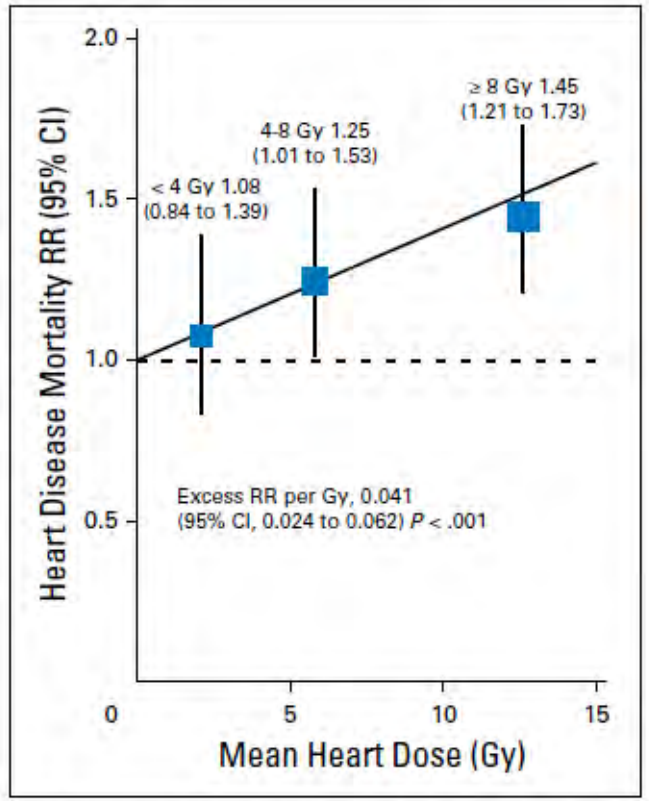


Fig 2. Heart disease mortality rate ratio (RR) by trial-specific mean radiation dose to the heart. The line was estimated using doses for individual women. Squares (with areas proportional to information content) show dose categories < 4, 4 to 8, and > 8 Gy, with mean doses of 2.1, 5.8, and 12.6 Gy.

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Estimating the Risks of Breast Cancer Radiotherapy: Evidence From Modern Radiation Doses to the Lungs and Heart and From Previous Randomized Trials

Cleveland Clinic 2016
Radiation-induced heart disease: a practical Guide to diagnosis and management

Complicanze Ischemiche nel Percorso Oncologico

- Esaminare sempre i fattori di rischio per CAD, considerando che alcuni chemioterapici sono di per sé un fattore di rischio
- Valutare in ogni paziente il rapporto costo/beneficio della radioterapia utilizzando la dose minore efficace e ponendo attenzione a dose cumulativa
- Cercare, nei pazienti ad alto rischio, una forma latente di CAD
- Monitorare strettamente per segni/sintomi di cardiopatia ischemica durante e dopo terapia con analoghi della pirimidina (fluorouracile),sospendendo se necessario
- Dopo complicanza tipo "spasmo coronarico", una nuova terapia va attuata solo se non ci sono alternative, pretrattando con nitrati e/o Cantagonisti
- Necessario lungo follow up se abbinate chemio e radioterapia

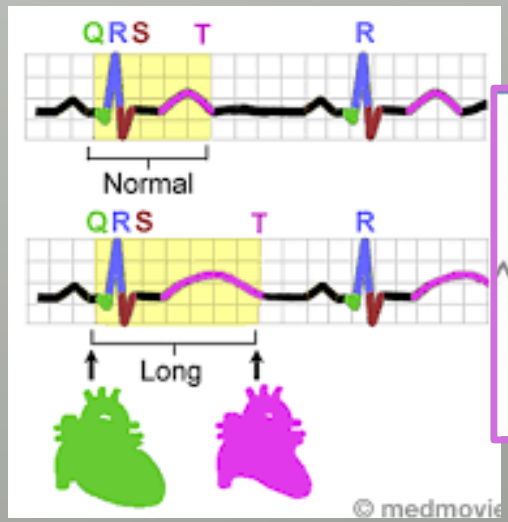
2016 ESC Position Paper on cancer treatments and cardiovascular toxicity

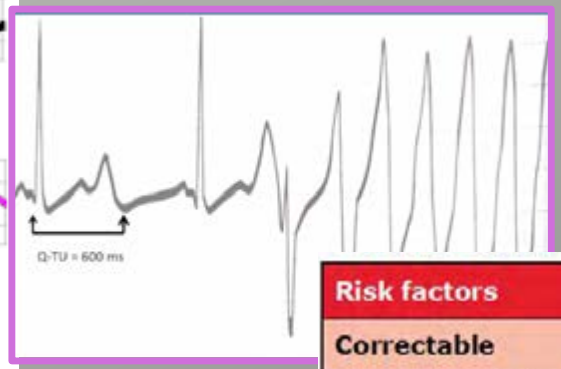
Complicanze Cardiovascolari nel Percorso Oncologico

- *Disfunzione ventricolare e scompenso*
- *Patologia Coronarica*
- Patologia Valvolare
- **Aritmie**
- *Ipertensione arteriosa*
- *Patologia Tromboembolica*
- *Patologia vascolare periferica e stroke*
- *Ipertensione polmonare*
- *Complicanze pleuropericardiche*

2016 ESC Position Paper on cancer treatments and cardiovascular toxicity

Complicanze Aritmiche nel Percorso Oncologico Esistono "fattori rosa"?





Risk factors	
Correctable	**Non-correctable**
Electrolyte imbalance • Nausea and emesis • Diarrhoea • Treatment with loop diuretics • Hypokalaemia (≤3.5 mEq/L) • Hypomagnesaemia (≤1.6 mg/dL) • Hypocalcaemia (≤8.5 mg/dL) **Hypothyroidism** **Concurrent use of QT-prolonging drugs** • Antiarrhythmic • Anti-infective • Antibiotic • Antifungal • Psychotropic • Antidepressant • Antipsychotic • Antiemetic • Antihistamine	• Family history of sudden death (occult congenital LQTS or genetic polymorphisms) • Personal history of syncope • Baseline QTc interval prolongation • Female gender • Advanced age • Heart disease • Myocardial infarction • Impaired renal function • Impaired hepatic drug metabolism

2016 ESC Position Paper on cancer treatments and cardiovascular toxicity

Complicanze Tromboemboliche nel Percorso Oncologico Esistono "fattori rosa"?

Cancer-related factors
- Primary site of cancer (mostly pancreas, brain, stomach, kidney, lung, lymphoma, myeloma)
- Histology (specially adenocarcinoma)
- Advanced stage (metastatic)
- Initial period after cancer diagnosis

Patient-related factors
- Demographics: older age, female sex, African ethnicity
- Comorbidities (infection, chronic kidney disease, pulmonary disease, atherothrombotic disease, obesity)
- History of venous thromboembolism, inherited thrombophilia
- Low performance status

Treatment-related factors
- Major surgery
- Hospitalization
- Chemotherapy and anti-angiogenic agents
- Hormonal therapy
- Transfusions
- Central venous catheters

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Conclusioni

La patologia tumorale non è più sempre una condanna, ma è aumentata la sopravvivenza spesso grazie alla cronicizzazione

- *Nel tumore della mammella la mortalità a 5 anni è ridotta drasticamente*
- *L'aumentata sopravvivenza ed i rischi tossici insiti nelle strategie*

Cardioncology: curing cancer saving the heart

➡ *Il rischio di evento cardiovascolare è aumentato in chi sopravvive a tumore mammario anche per la presenza di molti fattori di rischio in comune*

- *La gestione di queste pazienti deve uscire dai confini della cardiologia e dell'oncologia garantendo una reale interdisciplinarietà per poter massimizzare gli effetti delle terapie oncologiche minimizzando i rischi cardiovascolari*


Grazie per
l'attenzione!

Supplementary Table Most recent reviews and meta-analyses on the incidence of hypertension with major VEGF inhibitor treatment

Drug	Number of studies included	Number of patients	Incidence of all grades of HTN, %	Incidence of stage 3-4 HTN, %
Bevacizumab[165]	20	6754	23.6	7.9
Sunitinib[167]	13	4999	21.6	6.8
Sorafenib[168]	13	2492	15.3	4.4
Axitinib[169]	10	1908	40.1	13.1
Vandetanib[170]	11	3154	24.2	6.8
Regorafenib[171]	5	750	44.4	12.5

MedStar Health
Research Institute

Cardio-Oncology and Women's Heart Health: Optimizing Outcomes

Ana Barac, MD, PhD, FACC
MedStar Heart and Vascular Institute, Washington DC

Women's Heart and Vascular Conference, OhioHealth
January 30 2016

Rischio CTRCD dopo antiHER2 e inibitori VEGF

Agent	Risk factors
Anti-HER2 compounds	
– Antibodies - Trastuzumab - Pertuzumab - T-DM1 – Tyrosine kinase inhibitor - Lapatinib	• Previous or concomitant anthracycline treatment *(short time between anthracycline and anti-HER2 treatment)* • Age (>65 years) • High BMI >30 kg/mg^2 • Previous LV dysfunction • Arterial hypertension • Previous radiation therapy
VEGF inhibitors	
– Antibodies - Bevacizumab - Ramucirumab	Pre-existing HF, significant CAD or left side VHD (e.g. mitral regurgitation), chronic ischaemic cardiomyopathy • Previous anthracycline
– Tyrosine kinase inhibitors - Sunitinib - Pazopanib - Axitinib - Neratinib - Afatinib - Sorafenib - Dasatinib	• Arterial hypertension • Pre-existing cardiac disease

2016 ESC Position Paper on cancer treatments and cardiovascular toxicity

Table 1. Cancer Treatment and Cardiovascular Adverse Effects

Cancer Treatment	Cardiovascular Adverse Effects
Anthracyclines (eg, doxorubicin, epirubicin)	Left ventricular dysfunction, heart failure, myocarditis, pericarditis, atrial fibrillation, ventricular tachycardia, ventricular fibrillation
Alkylating agents (eg, cisplatin, cyclophosphamide)	Left ventricular dysfunction, heart failure, myocarditis, pericarditis, arterial thrombosis, bradycardia, atrial fibrillation, supraventricular tachycardia
Taxanes (eg, paclitaxel)	Bradycardia, heart block, ventricular ectopy
Antimetabolites (eg, 5-fluorouracil, capecitabine)	Coronary thrombosis, coronary artery spasm, atrial fibrillation, ventricular tachycardia, ventricular fibrillation
Endocrine therapy (eg, tamoxifen, anastrozole, letrozole)	Venous thrombosis, thromboembolism, peripheral atherosclerosis, dysrhythmia, valvular dysfunction, pericarditis, heart failure
HER-2–directed therapies (eg, trastuzumab, pertuzumab)	Left ventricular dysfunction, heart failure
Cyclin-dependent kinase 4/6 inhibitors (eg, palbociclib, ribociclib)	QTc prolongation
Radiation therapy	Coronary artery disease, cardiomyopathy, valvular disease, pericardial disease, arrhythmias

Potential cardiotoxicities of breast cancer treatment. QTc indicates corrected QT interval.

	Women without Breast Cancer (n=1,411)	Breast Cancer Survivors (n=1,413)
Deaths from any cause	242	415
Deaths from CVD[a]	105	133
Deaths from Breast Cancer[a]	2	135
Menopausal status		
Premenopausal, No. (%)	485 (34)	466 (33)
Postmenopausal, No. (%)	926 (66)	947 (67)
Ever used hormone replacement therapy		
No	1,073 (76)	1,033 (73)
Yes	338 (24)	408 (27)
Smoking		
Never	177 (13)	161 (11)
Passive exposure only	465 (33)	464 (33)
Ever active smoker only	132 (9.4)	133 (9.4)
Both active and passive	637 (45)	655 (46)
Alcohol intake, Lifetime average g/day		
Non-drinker	551 (39)	550 (39)
0-15	672 (48)	651 (46)
15-30	107 (7.6)	142 (10)
>=30	81 (5.7)	70 (4.9)
BMI[b] (kg/m^2) in year before reference date[b]		
<18.5	31 (2.2)	25 (1.8)
18.5-24.9	662 (47)	629 (44)
25.0-29.9	415 (29)	450 (32)
≥30.0	303 (22)	309 (22)
Hypertension		
No	946 (67)	925 (65)
Yes	465 (33)	488 (34)
Diabetes		
No	1,313 (93)	1,285 (91)
Yes	98 (6.9)	128 (9.1)
High Cholesterol		
No	980 (69)	988 (70)
Yes	431 (30)	425 (30)
Myocardial Infarction		

Table 2. Risk for Developing Cardiac Dysfunction

At-risk therapies including any of the following:
High-dose anthracycline therapy: doxorubicin ≥250 mg/m^2 or epirubicin ≥600 mg/m^2
High-dose radiation therapy when heart is in the field of treatment: radiotherapy ≥30 Gy
Sequential treatment: lower-dose anthracycline therapy (doxorubicin <250 mg/m^2 or epirubicin <600 mg/m^2) and then subsequent treatment with trastuzumab
Combination therapy: lower-dose anthracycline (doxorubicin <250 mg/m^2 or epirubicin <600 mg/m^2) combined with lower-dose radiation therapy when heart is in the field of treatment (<30 Gy)
Presence of any of the following risk factors in addition to treatment with lower-dose anthracycline or trastuzumab alone:
Older age at time of cancer treatment (≥60 y)
≥2 CVD risk factors during or after cancer treatment: diabetes mellitus, dyslipidemia, hypertension, obesity, smoking
History of myocardial infarction, moderate valvular disease, or low-normal left ventricular function (50%–55%) before or during cancer treatment

Cancer patients are considered to be at an elevated risk for developing cardiac dysfunction if they meet any of the criteria in this Table.

Adapted with permission from Armenian et al.[11]

CARDIOLOGICAL MONITORING IN PATIENTS UNDERGOING CANCER THERAPY

Patients at standard cardiac risk

According to the American College of Cardiology and American Heart Association (ACC/AHA) guidelines, patients receiving chemotherapy may be considered a Stage A HF group, defined as those with increased risk of developing cardiac dysfunction

Patients at increased cardiac risk

- Age < 18 or > 70 yrs
- Previous diagnosis of:
  - coronary artery disease
  - dilated/hypokinetic cardiomyopathy
  - diabetes mellitus
  - LVEF < 55% from any case
  - previous LVEF drop during or after CT
  - arrhythmias requiring treatment
  - valve disease - degree > moderate
- Previous or scheduled AC therapy > 300 mg/mq
- Previous mediastinum RT

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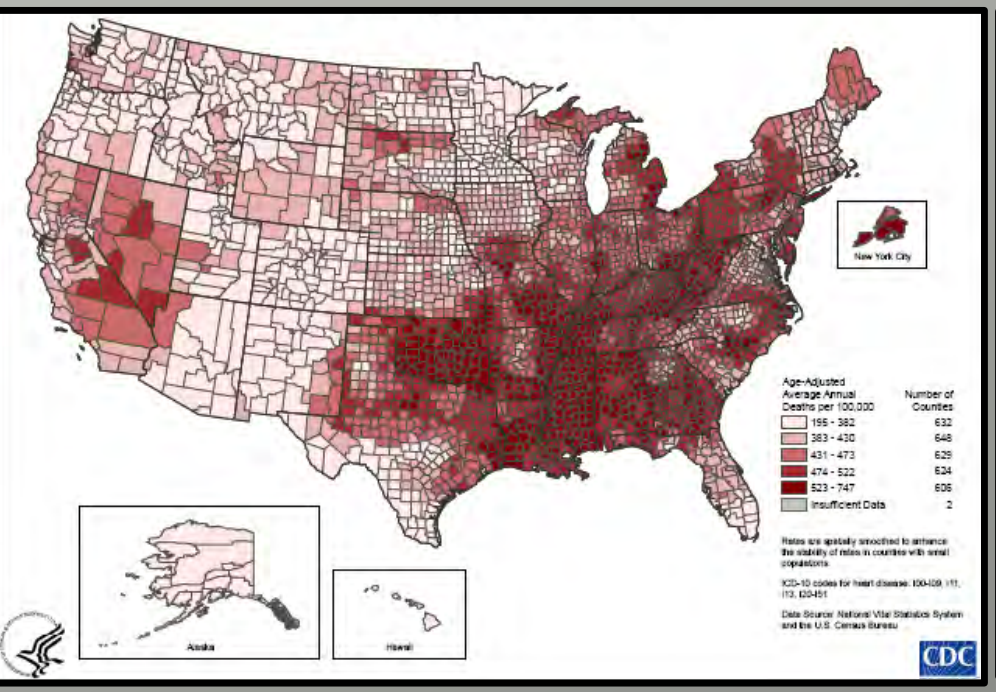
WILEY CLINICAL CARDIOLOGY

REVIEW

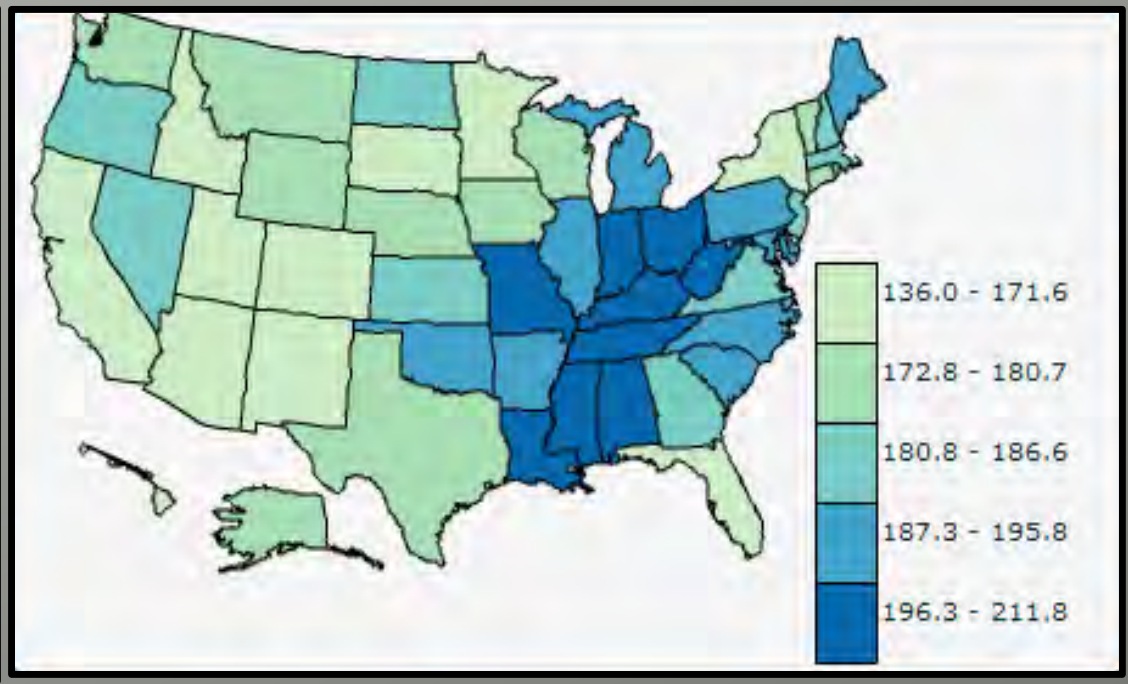
The connection between the breast and heart in a woman: Breast cancer and cardiovascular disease

Martha Gulati[1] | Sharon L. Mulvagh[2]

Mortalità
Cancro e Malattie Cardiovasocolari



Mortalità Cardiovascolare



Mortalità per Tumore

Rischio di Complicanze Cardiovascolari nel Percorso Oncologico
Esistono "fattori rosa"?