

AZERBAIJAN CARDIOLOGY FESTIVAL 13TH NATIONAL CONGRESS OF CARDIOLOGY 13 DECEMBER, 2024, BAKU

Heart failure in cancer patients — a problem of the 21-st century. Common pathogenesis and approaches to treatment

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Professor



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- Editor-in-Chief of the journal «Kardiologiia»

IC-OS International Cardio-Oncology Society [™] [™] [™] [™]





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)



ESC GUIDELINES

2022 ESC Guidelines on cardio-oncology developed in collaboration with the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS)

Developed by the task force on cardio-oncology of the European Society of Cardiology (ESC)



A unique edition. Fundamental work on heart failure 2023

12.13

Cancer and heart failure Dimitrios Farmakis*, Alexander Lyon*, Rudolf de Boer, and Yuri Belenkov

Introduction

Cancer is increasing in prevalence as a comorbidity affecting heart failure (HF) patients This has been attributed to several factors:1-3

- (i) shared risk factors, such as ageing, smoking, obesity;
- (ii) increasing survival of HF patients who can live to develop cancer;
- (iii) frequent use of cross-sectional imaging and contact with healthcare profession that results in increased cancer detection;
- (iv) common prescription of anticoagulation and/or antiplatelet agents unmasicancer due to the detection of bleeding or iron deficiency;

(v) emerging evidence that HP hadf may per as increase the risk of new cancer devi-

HEAT Failure Association The ESC Textbook of Heart Failure

Edited by Petar M Seferović Andrew JS Coats Gerasimos Filippatos Stefan D Anker Johann Bauersachs Giuseppe Rosano

ACADEMIC.OUP.COM/ESC

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Scientific Statement from the Heart Failure Society of America 2024.

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Journal of Cardiac Failure 00 (2024) 1-41



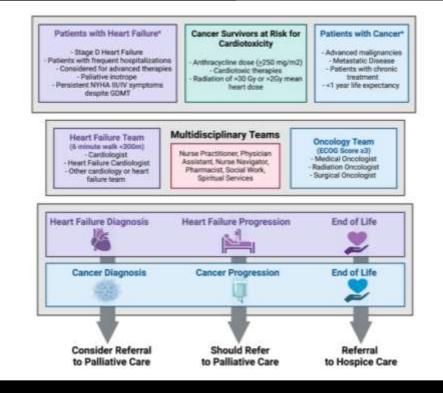
JCF

Review Article

Cardio-Oncology and Heart Failure: a Scientific Statement From the Heart Failure Society of America

MICHELLE WEISFELNER BLOOM, MD, Co-Chair¹ JACQUELINE B. VO, PhD, RN, MPH² JO E. RODGERS, PharmD, BCPS, BCCP³ ALANA M. FERRARI, PharmD, BCOP⁴ ANJU NOHRIA, MD, MSc⁵ ANITA DESWAL, MD, MPH[®] RICHARD K. CHENG, MD, MSc⁷ MICHELLE M. KITTLESON, MD, PhD[®] JENICA N. UPSHAW, MD, MS⁹ NICOLAS PALASKAS, MD¹⁰ ANNE BLAES, MD, MS¹¹ SHERRY-ANN BROWN, MD, PhD¹² BONNIE KY, MD, MSCE³³ DANIEL LENIHAN, MD¹⁴ MATHEW S. MAURER, MD¹⁵ ANECITA FADOL, PhD, NP¹⁴ KERRY SKURKA, RN, BSN¹⁷ CHRISTINE CAMBARERI, PharmD, BCOP¹⁸ CYNTHIA CHAUHAN, MSW¹⁹ and ANA BARAC, MD, PhD, Co-Chair²⁰

New York, NY; Bethesda, MD; ChapelHill, NC; Charlottesville, and Falls Church, VA; Boston, MA; Houston, TX; Seattle, WA; Los Angeles, CA; Minneapolis, and Rochester, MN; Milwaukee, WI; Philadelphia, PA; Tampa, FL



Karciologiya

Cardiotoxicity



Oncological process



therapy

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Specific antitumor therapy (polychemotherapy/radiation therapy)

Endothelial dysfunction (inhibition of proliferation and migration, apoptosis)

Cytokine imbalance (↑ TNF-α, TGF-β1, IL-1, IL-6)

Structural changes in cardiomyocytes (direct cardiotoxic effect, apoptosis) Vascular wall, Including the microcirculatory bed Myocardial remodeling Vasculotoxicity Cardiotoxicity

Remodeling of the

Camilli et al Cantio-Oncology (2024) 10:18 Miles (Max. et al 73, 113M/r40088-024-02718-0 Cardio-Oncology

Open Access

RESEARCH

Inflammation and acute cardiotoxicity in adult hematological patients treated with CAR-T cells: results from a pilot proof-of-concept study

Maximiliano Camili ¹², Marcello Vacovo¹, Tamara Felici¹, Luca Maggio¹, Federico Ballacci², Giacomo Caella², Alce Bonanni , Priscilia Lamendola¹, Lorenzo Trel², Antonio Di Renzo¹, Guila Coaell², Eugenio Gall¹⁴, Giovanna Luczo¹², Francesco Blazotta¹², Rocco Antonio Montone¹, Federica Sol^{34,1}, Simona Sca¹⁴, Solon Induau¹², Galatano Antonio Lanza¹², Rippo Ceal¹², Antone BL Jonbardo¹²⁸, and Giorgio Minetti¹³⁹

Abstract

Altras Chemics: Arright Receptor F (2047) call industry is a single evolving antitumer thesay, however, catalivascular (V) complications (rule) associated with cyclotion release updomer (202) and generic influenzation, have been reported to occur. The CAMdo-Tox study enred at elucideing incidence and determinants of cardiotaxicity rated to CAMT-call theory.

Methods: Fatients with blood naligrancies candidate to CART cells were propertiesly invaluated by enchandinguaphy baseline and 7 and 26 days after hankon. The tarky employtism were locations of naror through-related carbic dynkurction CERCU, CERCU were also balanced for any galed CRS. but CERCD occurred of Cardiology Cardiolities and Cardio-Concelogy Electrometries of electronic relativity properties long/balleria strain 63,53 and/or elevations of carbic promotion Psyls sensitivity trappenis L nativities peptideo and By, constations of educated popular institutions relative trappenis and the concellence of the centers with infiltermativity Sionara lens.

Results: Incidence of CTRCD was high at 7 days (94,7%), particularly in subjects with CRC. The integrated definition of CTRCD allowed the identification of the magnity of cases (50%). Moreover, early CPE and GLS decomments were inversely constant with fibritragen and interimulati-2 receptor levels (p always color). **Candiculsos:** There is a high incidence of early CTRCD in patients toward with CAPT cells, and a link between CTRCD and allowed with colors.

and information can be demonstrated. Dedicated patient monitoring protocols are advised.

Antonella Lambardo and Gargio Minutti share senior co- authorikija
*Comepondence Massimilano Camili massimilano camiliti digmal.com
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Peng et al. Cardio-Oncology (2024) 10:59 https://doi.org/10.1186/s40959-024-00264-8

RESEARCH

Cardio-Oncology

Open Access

Cardiovascular and venous thromboembolism risks in cancer patients treated with immune checkpoint inhibitors compared to non-usersa multi-center retrospective study

Jian-Rong Peng^{12,3}, Jason Chia-Hsun Hsleh³⁴, Chih-Hao Chang^{3,5,6}, Chi Chuang^{1,2,3}, Yu-Ching Wang⁷, Tzu-Yang Chen¹, – Hung-Chi Su^{1,2,3} and Hsin-Fu Lee^{1,2,3,4}

Abstract

Background - mmune Checkpoint inh bitors (ICIs) have revolutionized cancer therapy This study examines the cardiovascular risks of ICIs compared to non-ICI therapies.

Methods: Utilizing the Chang Gung Research Database (CGRD) of Taiwan, this retrospective study analyzed 188,225 cancer patients, with 1,737 undergoing (CI treatment from January 1, 2008, to June 30, 2021. Through 11 propensity score matching (PSM), we compared specific outcomes between patients treated with (CIs and Hose who were not. The analysis also accounted for the competing risk of mortality in assessing the results after PSM. The observation period spanned from this index date to which ever came first, the date of the specific outcomes, the last follow-up recorded, or the end date of the study on June 30, 2022.

Results: The study found no significant increase in the risk of cardiac death, non-fati imyocardial infarction, heart failure hospitalization, deep ven thrombosis, or purimonary embolism in patients treated with ICB as compared to those receiving non-ICI therapy. Interestingly, CI treatment was linked to a lower risk of non-fatal stroke (02.7% per year vs. 0.46% per year, subdistribution hazard ratio = 0.5% 95% confidence interval = 0.35 -0.98, P=0.0430). Furthermore, subgroup analysis revealed that the ICI group had a decreased risk of cardiac death in patients with cancers other than head and neck cancer, and a reduced risk of stroke among diabetic patients.

Conclusions: ICIs do not significantly elevate the risk of cardiovascular events in cancer patients and may lower the stroke risk, underscoring the need for additional prospective studies to clarify these findings.

Keywords Immune checkpoint inhibitor, Cancer, Stroke, Myocardial infarction, Heart failure, Deep vein thrombosis, Pulmonary embolism

*Commpiondence: Hsin-Fu Lae Hsinfu keeBigmall.com; 8805033@cgmn.org.tw Full list of author information is available at the end of the article

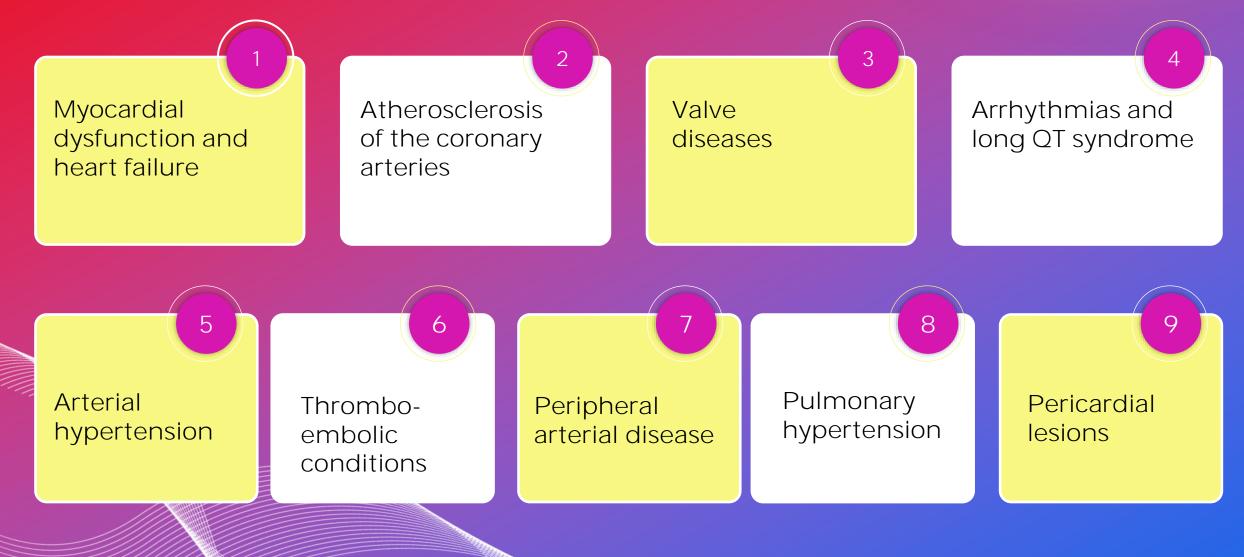


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McDonagh TA, et al. 2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2023 Aug 25:ehad195. doi:/10/1093/eurheartj/ehad195

Clinical manifestations of cardio-vasculotoxicity



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CANCER

Cell division

Increased cell number

Angiogenesis

Increased metabolic activity

Drug/toxin resistance



Heart failure

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Failure of cell division/ tissue repair

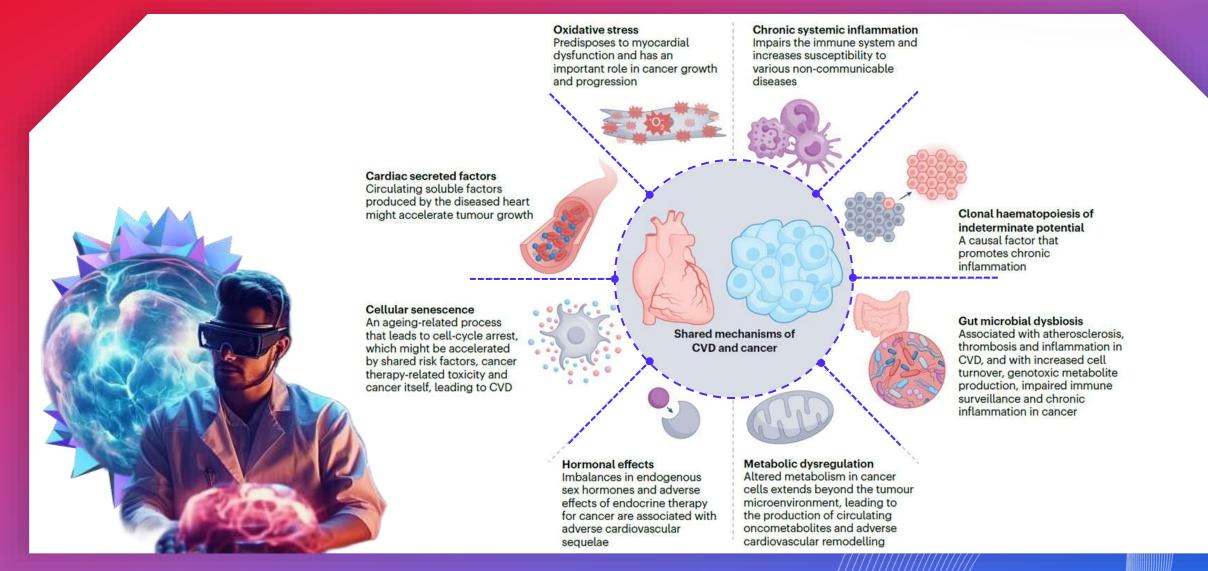
Cell loss

Ischaemia

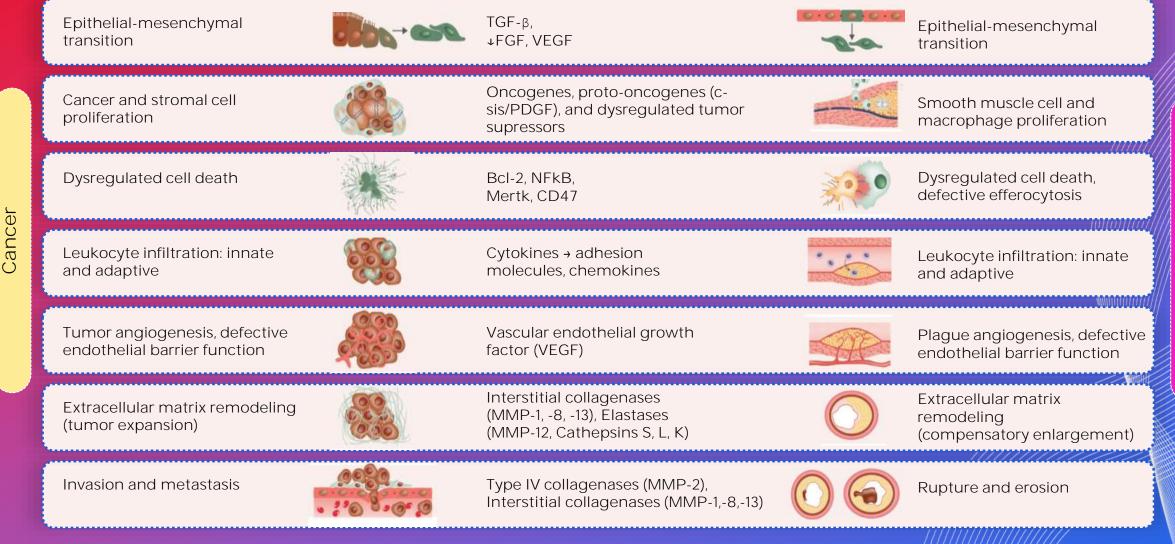
Impaired/decreased energetic efficiency

Increased sensitivity to toxins

Cardio-Oncology Balance Shared Pathophysiological Mechanisms



Chronic pro-inflammatory status: shared pathophysiological pathways



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The link between heart failure and cancer risk factors

Common risk factors (smoking, diet, obesity, poor lifestyle)

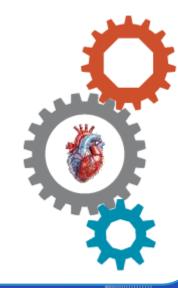


Shared pathophysiological pathways:

- Inflammation;
- Clonal hematopoiesis of indeterminate potential;
- Angiogenesis;
- Extracellular matrix/microbiome

Secreted /circulating factors

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Journal of Canolise Failure 00 (2024) 1-8



Brief Report

Cardio-Oncology and Heart Failure: AL Amyloidosis for the Heart Failure Clinician: a Supplement to the Scientific Statement from the Heart Failure Society of America

MICHELE WESPELIKE BLOOM, MD, Co-Char¹ ACQUELINE B, VO, PRO, INN, MPH² JOE, RODGRES, Pharmo, DCF, SCO² HAAAM, MI, TERMAR, Thuman, DCCP⁴ ANI, MOHBA, MD, MS² ANITA DESWAL, MD, MPH² ROLAND, USA, CHENG, MD, MS² MICHELE M, KITTESON, MD, MP³ JENCAN, USPWAW, MD, MS² MICOLAS PALAGKIS, MD¹⁹ ANNE BLASS, MD MS³ SHEBY-ANN BROWN, MO, HO³¹ BONNE KY, MD, MSCE³³ DANEL, LINHAM, MD³¹ MATHERY KI MAURER, MO⁴¹ ANECTA FADOL, PHO, MSCE³³ KIBHY SKIRKA, RH, BSM³² CHRISTINE CAMBARER, PharmO, BCOP³⁴ and ANA BARKE, MD, HD, Co-Char³²

New York, New York, Berlevale, Maryland, Chapel Hill, Marth Casolina, Charlotterville and Falls Church, Vegenic, Boston, Masanchaette, Houston, Toxas, Seattle, Washington; Loz-Argeles, Californic, Minneapolis and Rochester, Minneapolis, Philadelphia, Perrephanic, and Tarepa, Roside

Key Wards: Heart failure, cancer, cardiotoxicity, cardio-ancellogy, cancer treatment-related cardiac dynanction, cardiomyoparty, heart failure with reduced ejection fraction, heart failure with preserved ejection fraction, bone manowhsem cell transplant, pulmonaw.

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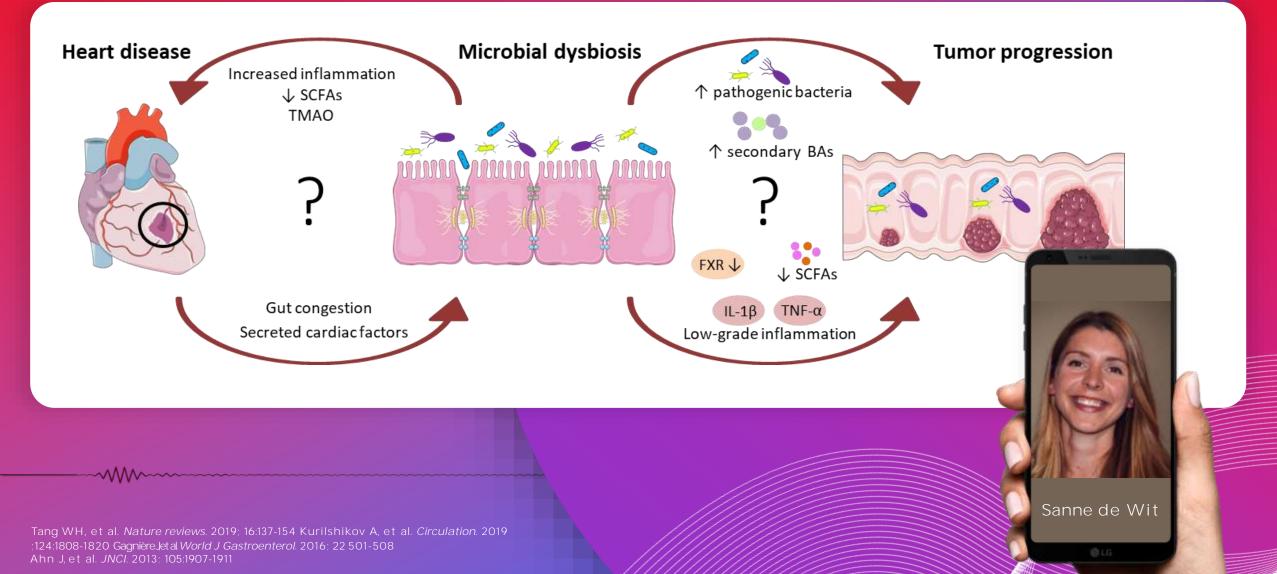


McDonagh TA, et al. 2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2023 Aug 25:ehad195. doi: 10.1093/eurheartj/ehad195

Forp et al. Cantio-Oncology (2100)-614 Cardio-Oncology 1/kbi.arg/10.1185/L40969-020-00088-6 RESEARCH Open Access ۲ Healthcare utilization and hospital variation in cardiac surveillance during breast cancer treatment: a nationwide prospective study in 5000 Dutch breast cancer patients Yvonne Koop⁷¹ Saloua El Messaoudi¹, Hester Verneulen^{1,1}, Angela H. E. M. Maas¹ and Fernie Atsma² Abstract Background: Various breast cancer (BC) treatments, such as chemotherapy and targeted therapies, increase cardiotoxicity-risk and lead to premature ischemic heart disease and heart failure among survivors. Reducing this adverse risk through early recognition and (preventive) treatment is therefore important. Conversely, we feel that creening for cardiotoxicity is currently insufficiently standardized in daily practice. A fundamental first step in identifying areas of improvement is providing an overview of current practice. Objectives This study aims to describe current cardiac surveillance for women with BC during and after cardiotoxic cancer treatment, using routinely collected hospital data in the Netherlands. The study also describes hospital variation in cardiac surveillance. Methods: This observational study was performed on claims data provided by Statistics Netherlands. From the data, newly diagnosed BC patients in 2013 (V = 16,040) were selected and followed up until 2015. Healthcare utilization analyses were performed for all cardiac and oncologic healthcare activities but with a specific focus on cardiac suneillance healthcare activities. In addition, differences between types and individual hospitals were evaluated. Results: Almost one third of all BC patients received high risk cardiotoxic treatments (V = 5157), but cardiac surveillance was savely performed. Cardiac care provided to patients mainly consisted of ECGs 52,0% and MUGA scars D5.5%. Cardiac MR was performed in 0.7% of the patients, echocardiography in 17.7%, and measurement of Troponin and NT-proBNP in 5.1 and 5.8%, respectively. Moreover, we observed a substantial variation in cardiac surveillance between different hospital types and between individual hospitals. Conclusion: This study shows that women treated for BC with cardiotoxic treatments do not receive recommended cardiac surveillance. Standardized approaches in clinical care are ladving, resulting in low rates of diagnostic testing and a substantial variation in susveillance between hospitals. A structured approach and increased interprofessional collaboration could lead to tailored cardiac surveillance for early detection of cardiotoxicity and therefore start of treatment. Keywords: Cardiac imaging, Epidemiology, Breast cancer, Cardiotoxicity, Quality of care, Health policy Department of Cardology, Radioud Lowenty Medical Center, Geor-Grootepien 10 - route II's, Postbus VIII's 500 Nijnegen, HE. The full lat of agthor information is available at the end of the article BANCO In the starting, starting star

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The relationship between CHF and microbiome



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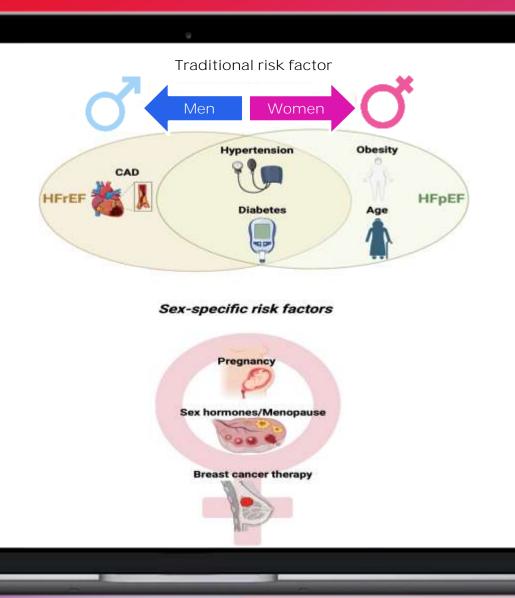
Interaction between HF, gut dysbiosis, cancer, and cancer therapy



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IC-OS International Cardio-Oncology Society

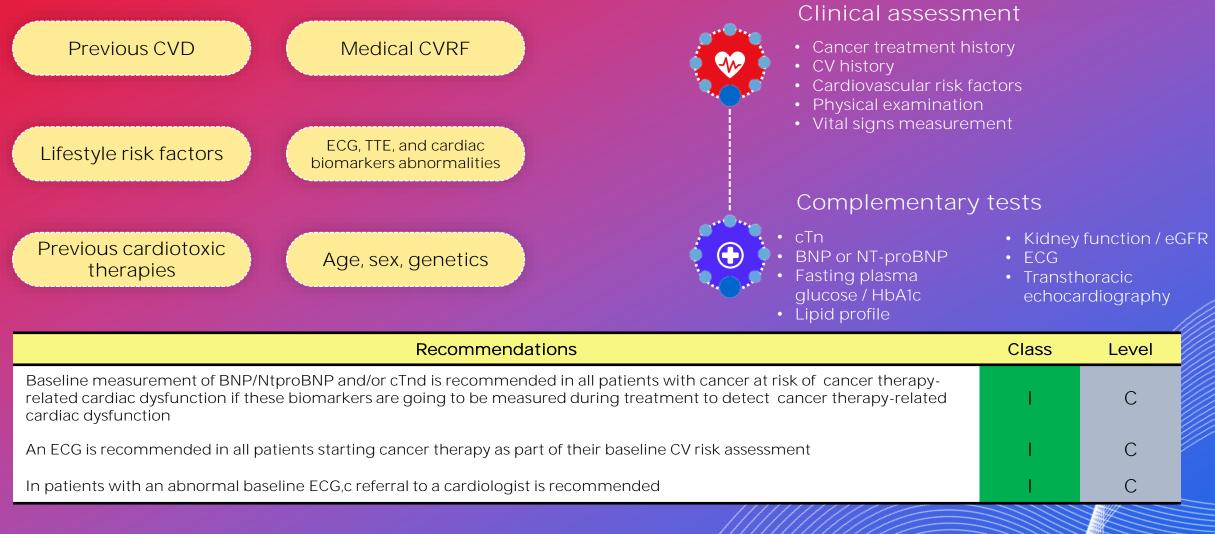
The main traditional and gender risk factors involved in the pathogenesis of HF with reduced and/or preserved ejection fraction





Шляхто Е.В., Беленков Ю. Н., Бойцов С.А., Виллевальде С. В., ГалявичА. С., Глезер М. Г., ЗвартауН. Э., КобалаваЖ. Д., Лопатин Ю.М., Мареев В.Ю., Терещенко С.Н., Фомин И.В., БарбарашО.Л., Виноградова Н. Г., Дупляков Д.В., Жиров И.В., Космачева Е. Д., Невзорова В. А., Рейтблат О.М., Соловьева А.Е., Зорина Е.А.Проспективное наблюдательное наблюдательное наблюдательное исследование пациентов с хронической сердечной недостаточностью в РФ ПРИОРИТЕТ-ХСН): обоснование, цели и дизайн исследования. Российский кардиологический журнал. 2023;28(6):5456. doi:10.15829/I560-4071-2023-5456

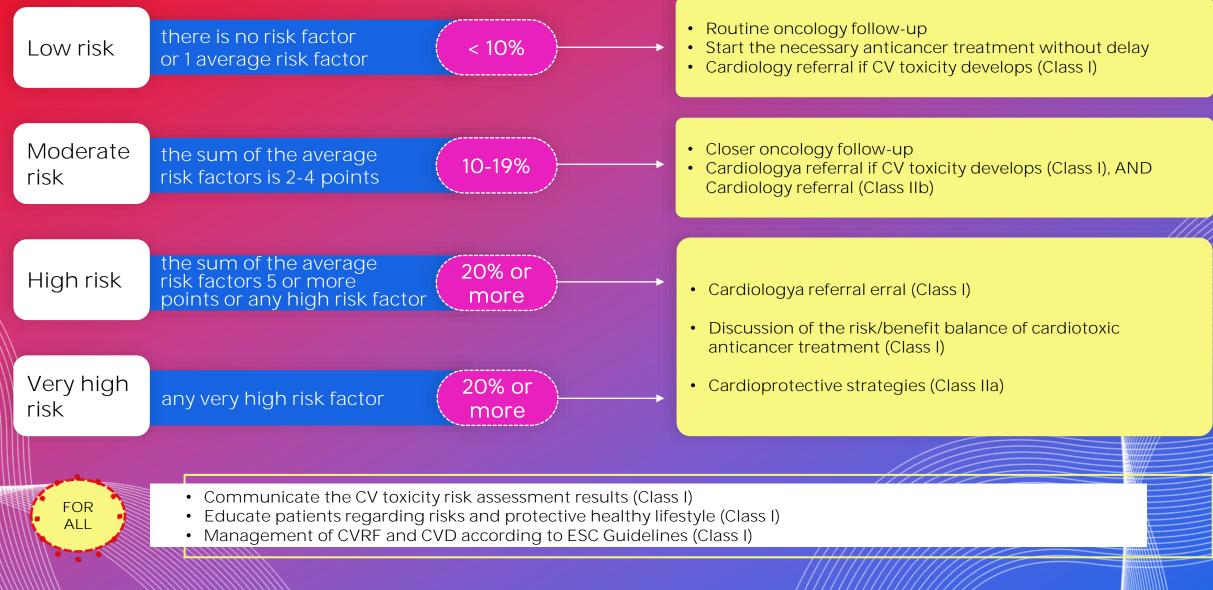
Cardiovascular toxicity risk stratification before anticancer therapy



Lyon, Alexander R et al. European heart journal vol. 43,41 (2022): 4229-4361. doi:10.1093/eurheartj/ehac244 /

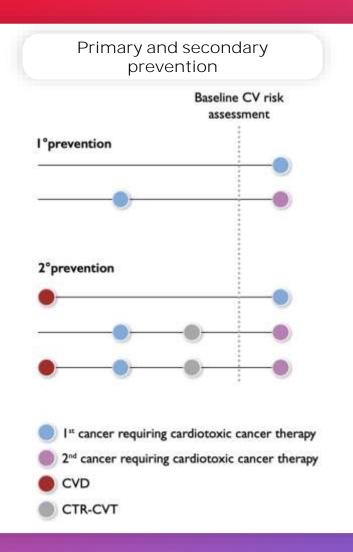
10-year risk of CV events

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Lyon Alexander R et al European heart journal vol. 43,41 (2022): 4229-4361. doi:10.1093/eurheartj/ehac244

Patient phenotypes and cancer-therapy related cardiovascular toxicity prevention strategies



Management of CVD and CVRF according to ESK Guidelines

In patients with high and very high risk of CTRCD

Minimize the use of cardiotoxic drugs

ACE-I/ARB and/or BB

Dexrazoxane/liposomal anthracyclines (patients treated with anthracyclines)

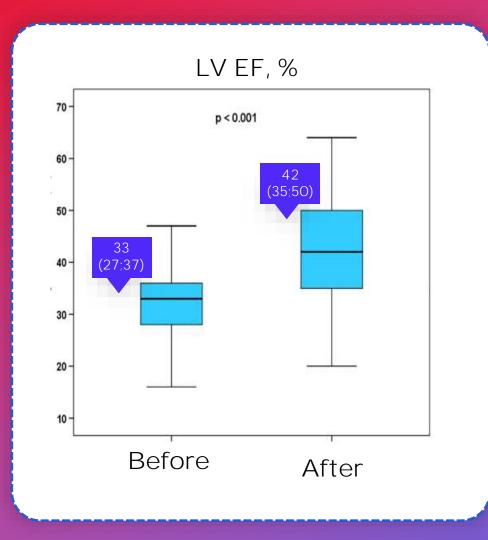
Statins

Management of CVRF according to the 2021 ESC Guidelines on CVD prevention in clinical practice is recommended before, during, and after cancer therapy (IC)

Class IIa

Class I

Sacubitril/valsartan in the treatment of PHT-associated cardiotoxicity and CHF



Criteria:



- n = 67, breast cancer, lymphoma
- 2
- PHT (70% with anthracyclines), RT



Median age 56.2±13.4 years



Cardiotoxicity with HF



Median LVEF 33%

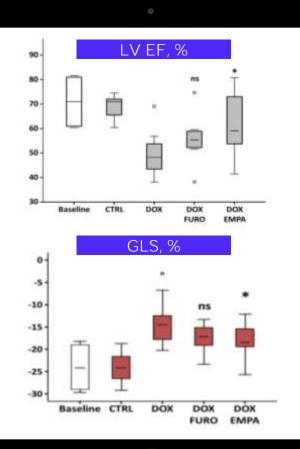


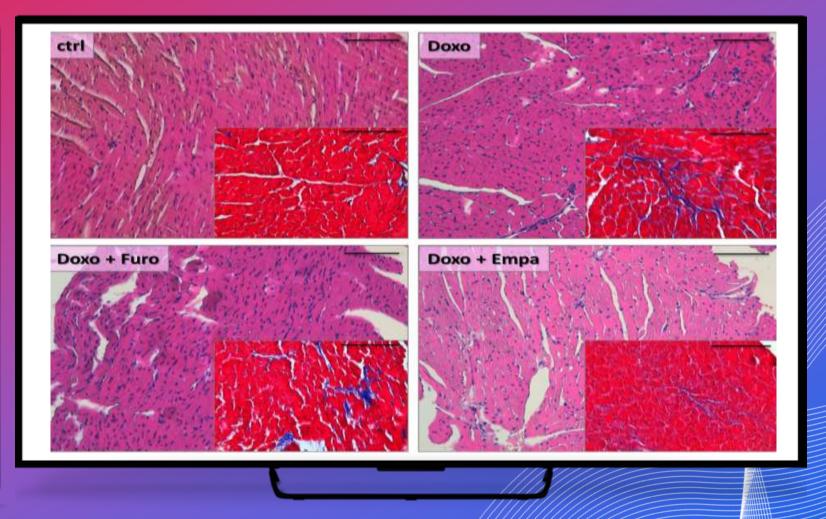
5 months follow-up



Combination therapy using sacubitril/valsartan

Empagliflozin for the prevention of DOX-associated cardiotoxicity (experimental model)

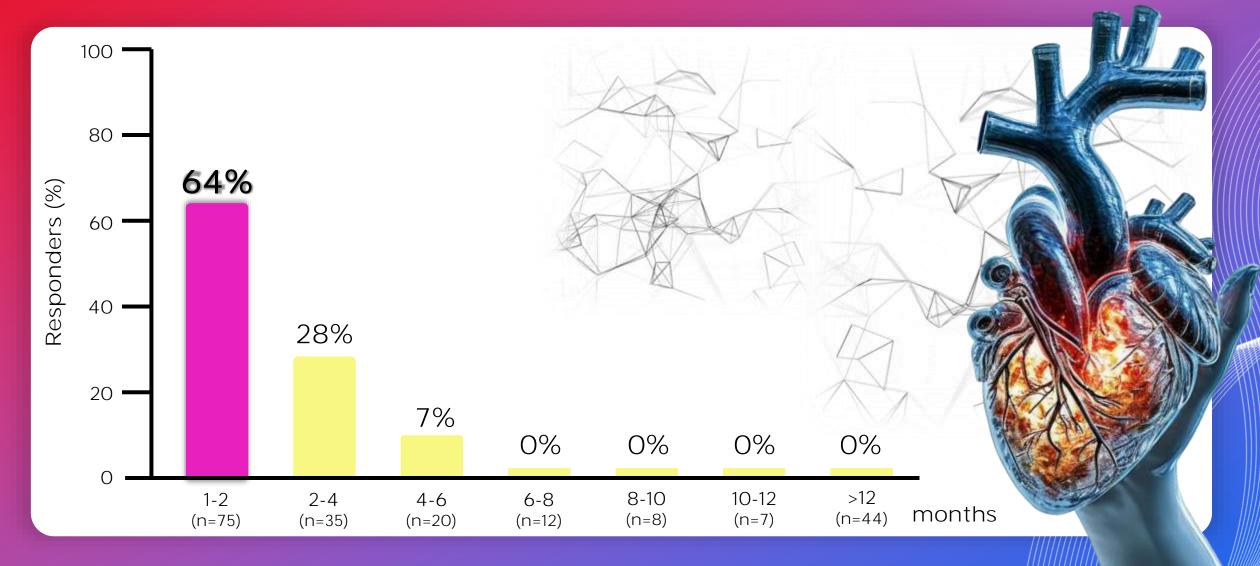




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Sabatino J. et al. Cardiovasc Diabetol, 2020

Early detection of cardiotoxicity is the key to a good prognosis



Kardiologiya

What is Reverse Cardio-Oncology? Cancer driving heart disease Heart disease driving cancer

	CVD	No CVD	P value‡
Sample size	4089	40 502	
Weighted sample size	127 809 316	1 610 614 001	
Age, y, median (IQR)	64.5 (53.7– 74.1)*	41.1 (28.9– 53.7)*	<0.0001*
Female sex, n (%)	59 525 877 (46.6)*	831329637 (51.6)*	<0.0001*





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Cardiovascular Diseases Increase Cancer Mortality in Adults: NHANES-Continuous Study

Cmar M, Makram, MD, MFH [®], Tochakwu Okwoosa, OO [®], Darlei Addison, MD [®], Jorge Corles, MD [®], Susan Dent, MD [®], Malcom Bevel, PhD, MSFH [®], Sarju Bosatra, MD [®], Sadeer Al-Kindi, MD [®], Catherine C Heckok, PhD [®], Neel L Weintrauti, MD [®], Xaoling Wang, MD, PhD [®], and Avirap Gute, MD, MPH [®] [®], <u>Authol aleba Artistations</u> Journal of the American Heart Association • Volume ¹3, Number 15 • https://doi.org/10.1103/JAHA.724.035500



Conclusion (NHANES – Continuous Study 2024)



The study shows

All cardiovascular individuals are at higher risk of cancer mortality. Individual risk factors, including smoking, aging, and obesity, also significantly contribute to cancer mortality in individuals with CVD. Our findings highlight the potentially important role of obesity in the link between CVD and cancer mortality



The role of obesity in this relationship requires further exploration in future studies

Future research should examine the impact of CVD severity, such as heart failure stage and the effect of various cardiovascular medication intake on cancer mortality

	CVD (N=127 809 316)	No CVD (N=1 610 614 001)	P value
Median follow-up years	9.8 (5.3–	10.2 (5.9–	<0.0001‡
(interquartile range)*	16.3) <mark>‡</mark>	15.6) <mark>‡</mark>	
No. of deaths due to cancer,	4 084 613	11 221 492	<0.0001‡
n (%)	(3.2)‡	(0.7)‡	

Accertosystem Karciologya

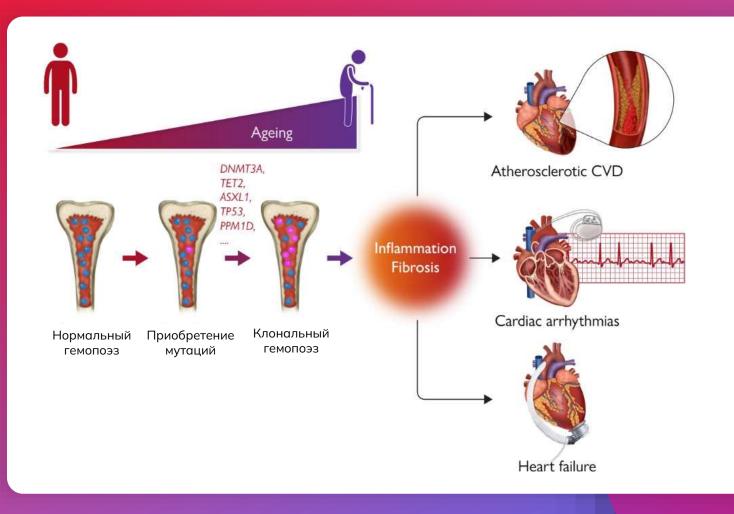


Atrial fibrillation and the risk of developing cancer in the future



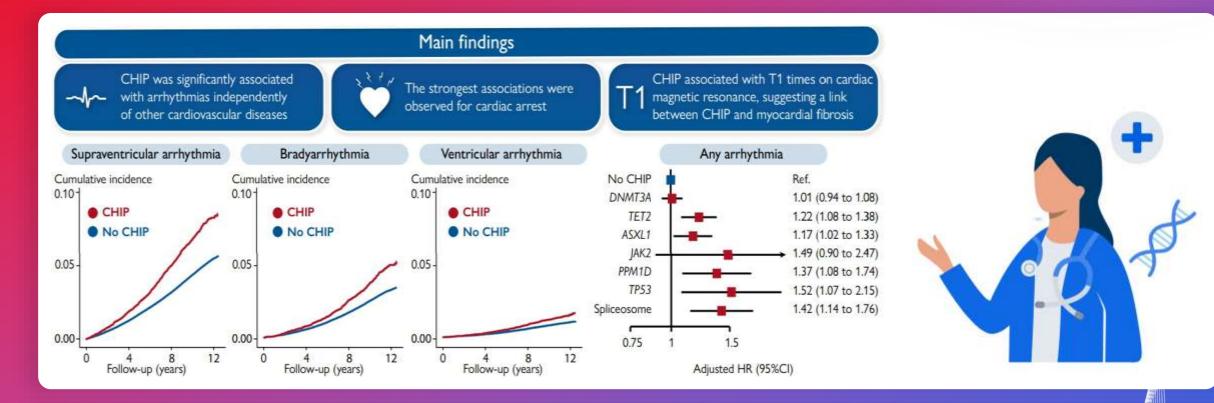
Azarbaytan Cardiologiya © ESC Cardiologiya Cardiologiya

Clonal hematopoiesis is a new risk factor for the development of cardiac arrhythmias





Clonal hematopoiesis is a new risk factor for the development of cardiac arrhythmias



Strong effects of mutations affecting the TP53 and PPM1D DNA damage response genes

These mutations are especially common among cancer patients and survivors

akostubo Syndrome and Cancer

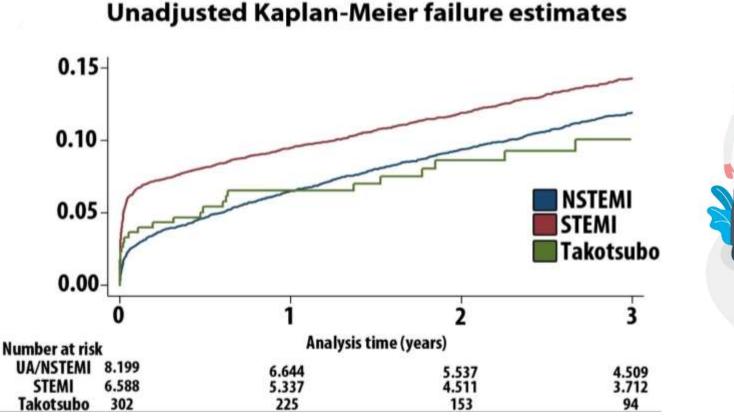
Prevalence of cancer in Takotsubo syndrome patients at presentation

Future cancer incidence in Takotsubo syndrome survivors



Mortality in Takotsubo syndrome is similar to mortality in myocardial infarction

Data from the SWEDEHEART registry





Azərbaycan Kərcilologiyə ESC Dernyyəti oʻzətisilər oʻzətisilər

Long term mortality in patients with Takotsubo syndrome

Overall long term mortality for Takotsubo syndrome :

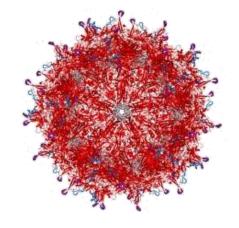
5,6% mortality per annum	in InterTAK registry	Non-CV causes
		> CV causes
Overall 20-25% 10 year mortality	deaths from all causes	
8% 3 year mortality	deaths from all causes in SWEDEHEART registry	

Acarbaycan Rarciologiya Carriyyaŭ ©ESC Europar Society or Carrielogy Increased incidence of de novo malignancies in patients with Takotsubo syndrome during long-term follow-up

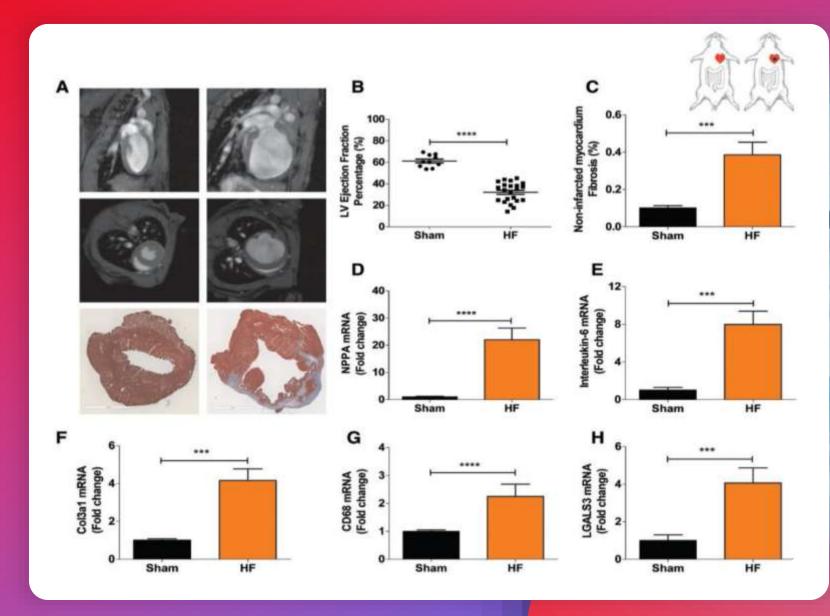
~8% of cancer patients suffer from paraneoplastic syndrome

The diagnosis of a new malignancy appears to be more common in patients with Takotsubo syndrome during follow-up:

- Casuistic nature;
- Small cohorts: 50 patients with Takotsubo syndrome vs. 50 patients with IM, follow-up period 2.9+/-1.6 years;
- 14% (7/50) vs 0% incidence of new cancer in Takotsubo syndrome vs IM1;
- Requires prospective study;
- Is Takotsubo syndrome a paraneoplastic syndrome in some cases?
- Is there cancer screening in patients with Takotsubo syndrome?
- Atypical or unusual cases:
 - Spontaneous Takotsubo syndrome;
 - Male patients with Takotsubo syndrome;
- Long-term follow-up is appropriate



HF Promotes Tumor Growth





Azərbaycan Karciologiya Cəmiyyəti ESC

T HER Barr Salar Salar

IC-OS International Cardio-Oncology

Meijers WC, et al. Circulation. 2018; 137:678-69

1. What mechanisms explain the Bidirectional Connection Between Cancer and HF?

2. Can we target these?



Shared Risk Factors (smoking, obesity, sedentary lifestyle, diet)



HF Secreted/Circulating Factors



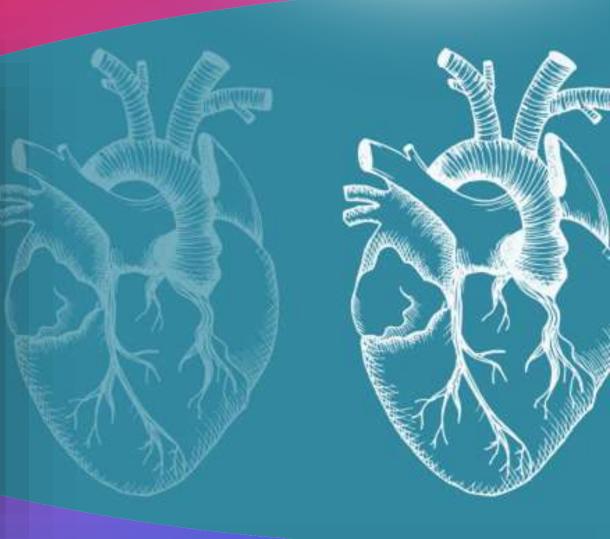
Shared Mechanisms:

- Inflammation
- Clonal Hematopoiesis of Indeterminate Potential
- Angiogenesis
- Extracellular Environment/microbiome

Summary

There is an increased risk of new cancer in a range of different CV populations MI, AF, ACHD, PH, Takotsubo syndrome

- Range of reasons
 - o Shared risk factors
 - o Shared pathophysiology
 - Increased medical investigations
 - Increased used of Anticoagulant or Antiplatelets and bleeding
- CV and Cancer survivorship both increasing



Bidirectional Cardio-Oncology

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Ping Pong Cardio-Oncology









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Thank you for attention!