

Cardio-oncologie

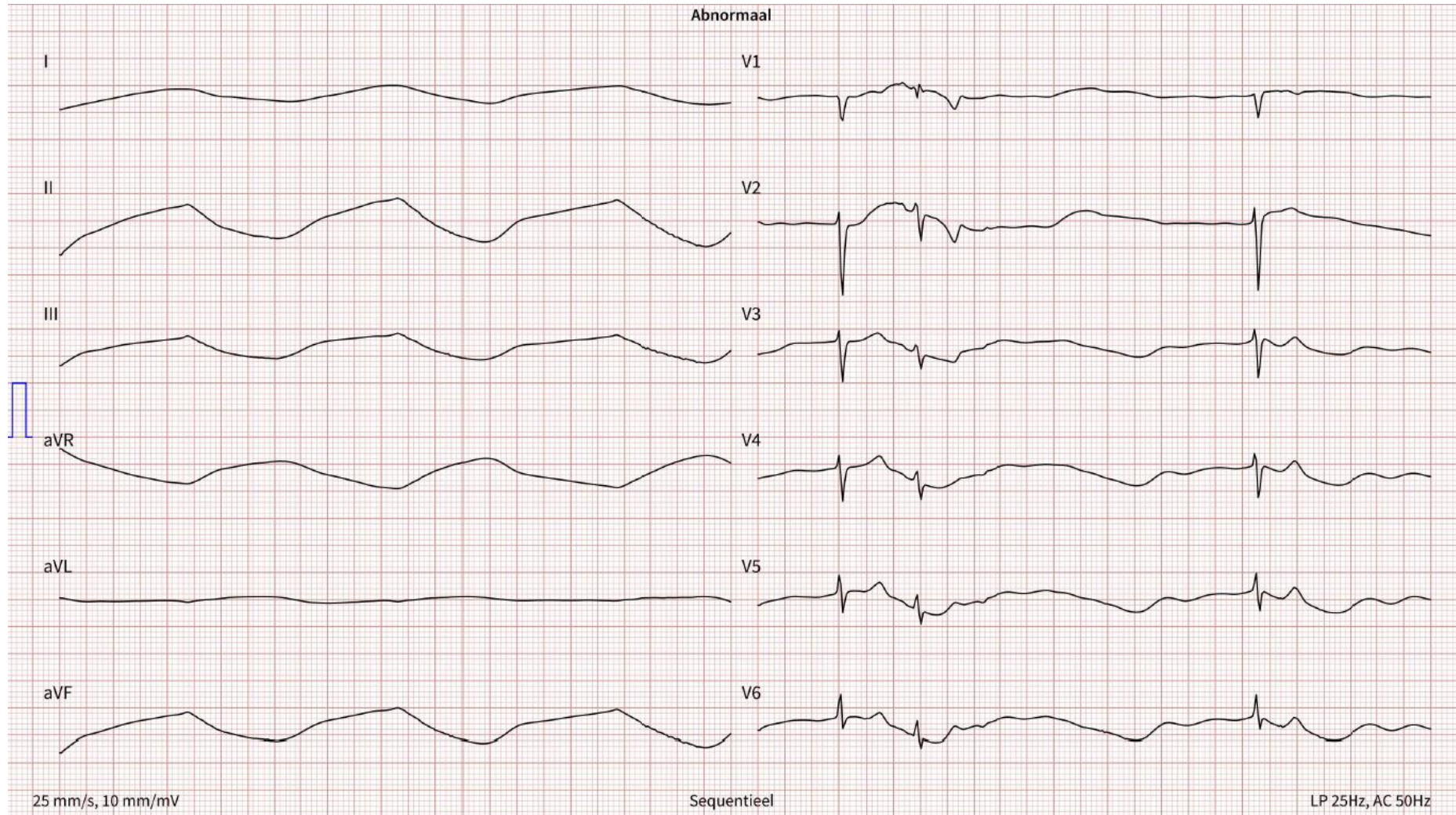
modeverschijnsel of levensnoodzakelijk?

Huisartsensymposium – januari 2023

dr. Philippe Mortelmans



Dringend ECG aan bed

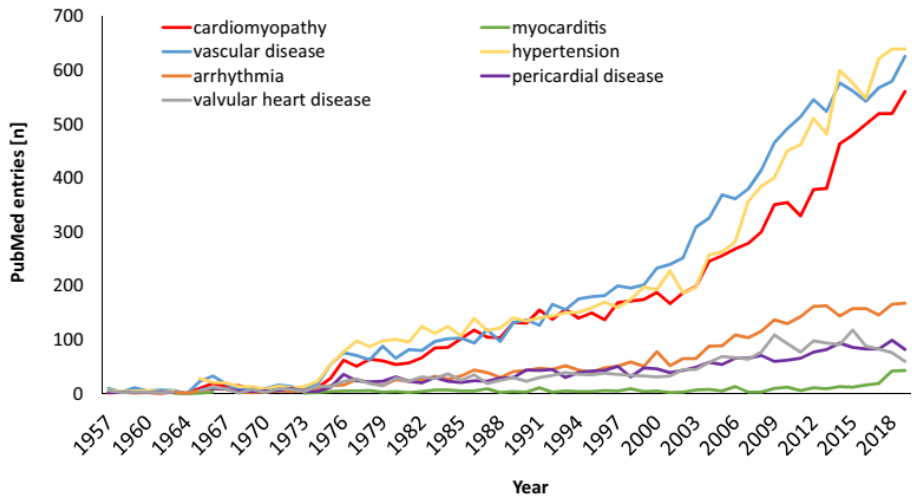



cardio-oncologie

WAT EN WAAROM?


jonge discipline

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



 **ESC**
European Society of Cardiology
European Heart Journal (2018) **00**, 1–8
doi:10.1093/eurheartj/ehy453

SPECIAL ARTICLE

 **ESC**
European Society of Cardiology
European Journal of Heart Failure (2020)
doi:10.1002/ejhf.1985

REVIEW

 **ESC**
European Society of Cardiology
European Journal of Heart Failure (2020)
doi:10.1002/ejhf.1920

POSITION PAPER

Baseline cardiovascular risk assessment in cancer patients scheduled to receive

 **ESC**
European Society of Cardiology
European Journal of Heart Failure (2020)
doi:10.1002/ejhf.2017

POSITION PAPER

Role of serum biomarkers in cancer patients receiving

 **ESC**
European Society of Cardiology
European Journal of Heart Failure (2020)
doi:10.1002/ejhf.1957

POSITION PAPER

Role of cardiovascular imaging in cancer patients receiving cardiotoxic therapies:



ESC

European Society
of Cardiology

European Heart Journal (2022) 43, 4229–4361

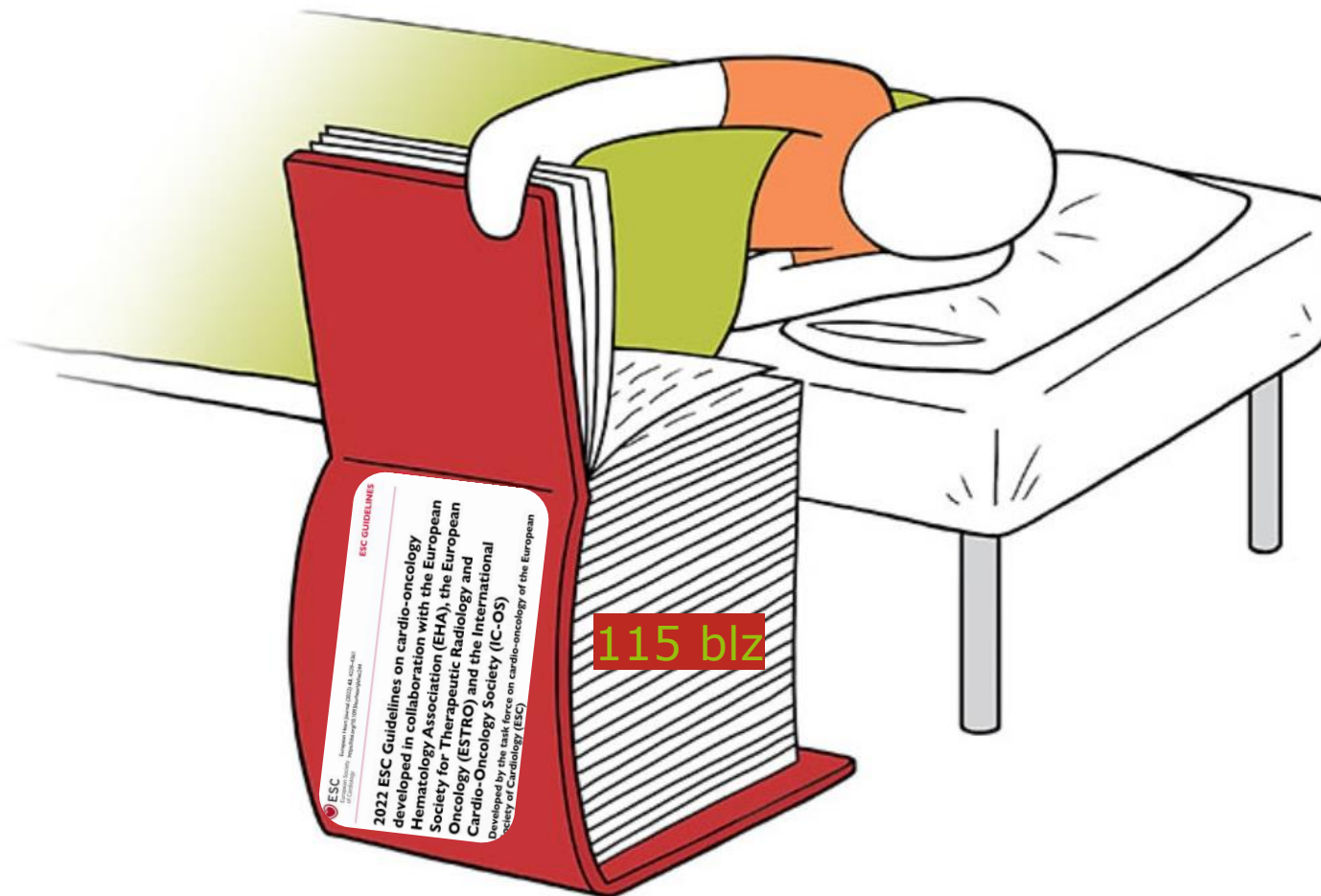
<https://doi.org/10.1093/eurheartj/ehac244>

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)**

2022 ESC guidelines on cardio-oncology



2022 guidelines on cardio-oncology: kritiek

"A large number of the recommendations are likely to not stand the test of time."



- te brede screening
 - vals +
 - vereist mankracht
 - duur
- lage bewijskracht
 - LoE A: 2.6%
 - LoE C: >75%

Wie volgt dit?

Juridische consequenties?

"What percentage of providers currently meet what is being recommended?"

If the number is <50%, most providers are by definition providing care below the "standard-of-care".

Waarom cardio-oncologie?

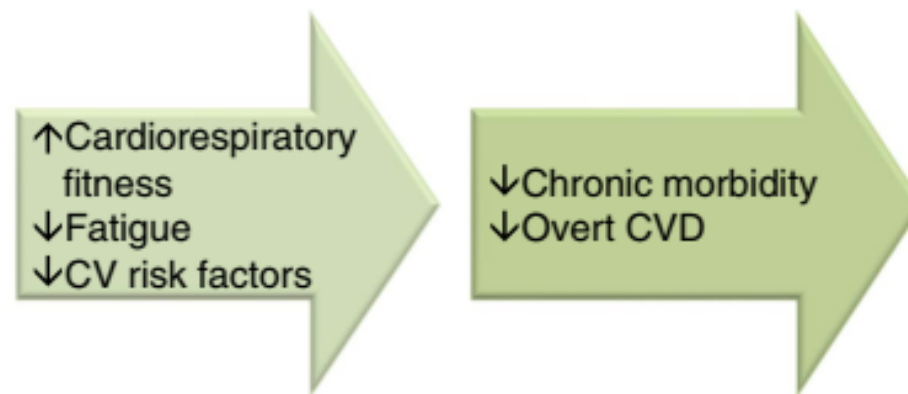
- overleving van zowel cardiovasculaire (CV) als oncologische aandoeningen verbetert
 - 2017: 62% van de overlijdens = c-v of kanker
- hartfalen en kanker: gemeenschappelijke
 - risicofactoren (obesitas, roken, leeftijd, alcohol, vervuiling, sedentair, ...)
 - symptomen (vermoeidheid, oedemen, vermagering, ...)
 - gevolgen (depressie, anemie, ijzertekort, cachexie, ...)
 - behandeling: bewegen!

- nieuwe kanker

Cardiac function	↑Stroke volume ↓Heart rate ↑Cardiac output
Arterial/endothelial function	↑NO ↑Angiogenic factors
Skeletal muscle function	↑Mitochondrial size and number ↑Capillarization

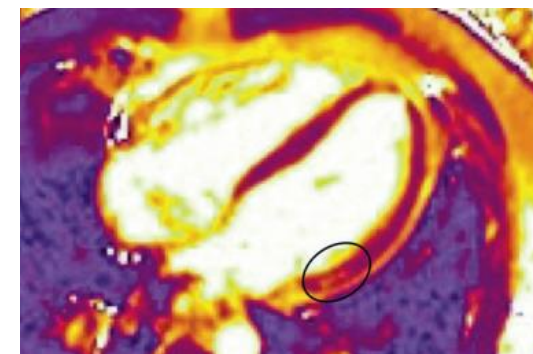
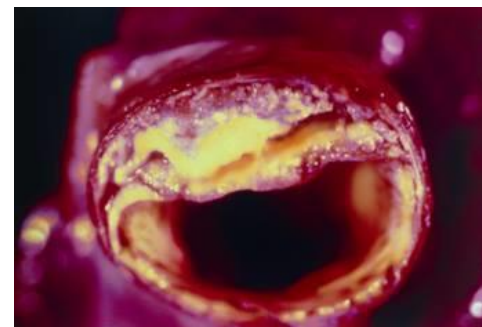
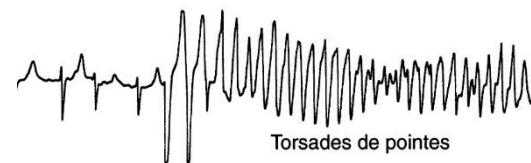
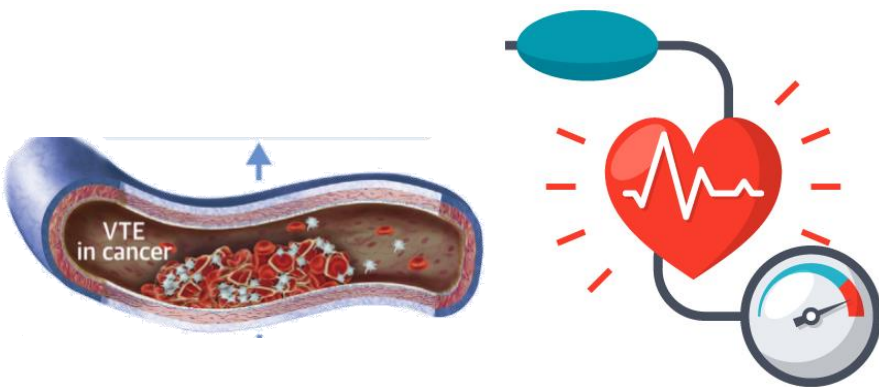
- → aantal patië

- GZA: sterk uit



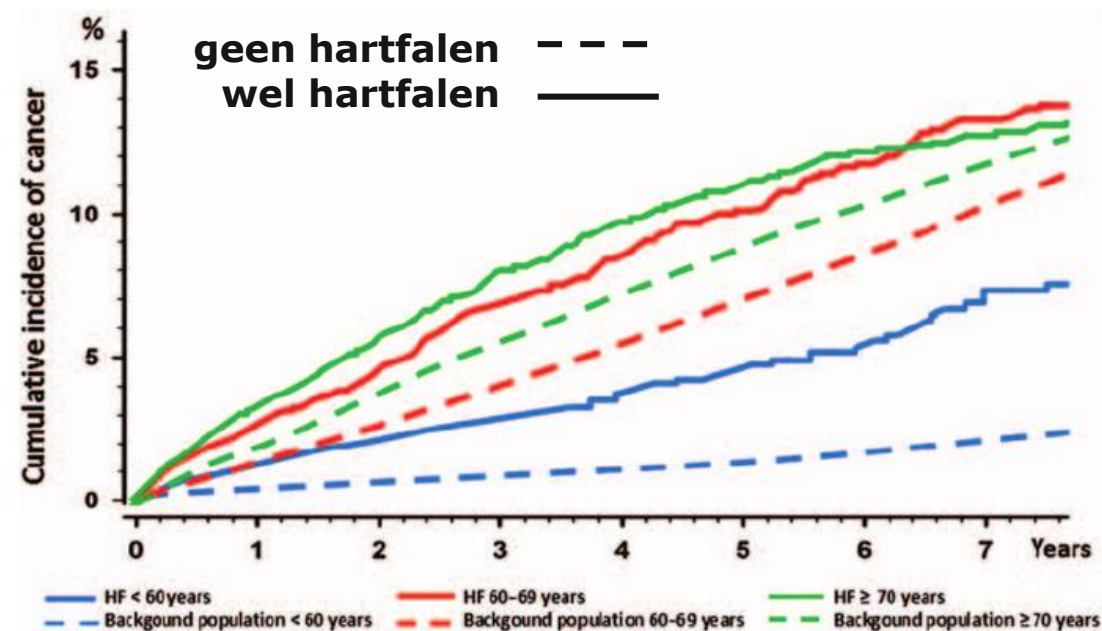
Wat weten we?

- anthracyclines en Herceptine
- MAAR
 - niet enkel linkszijdig hartfalen
 - hartfalen $\leq ? \geq$ kanker



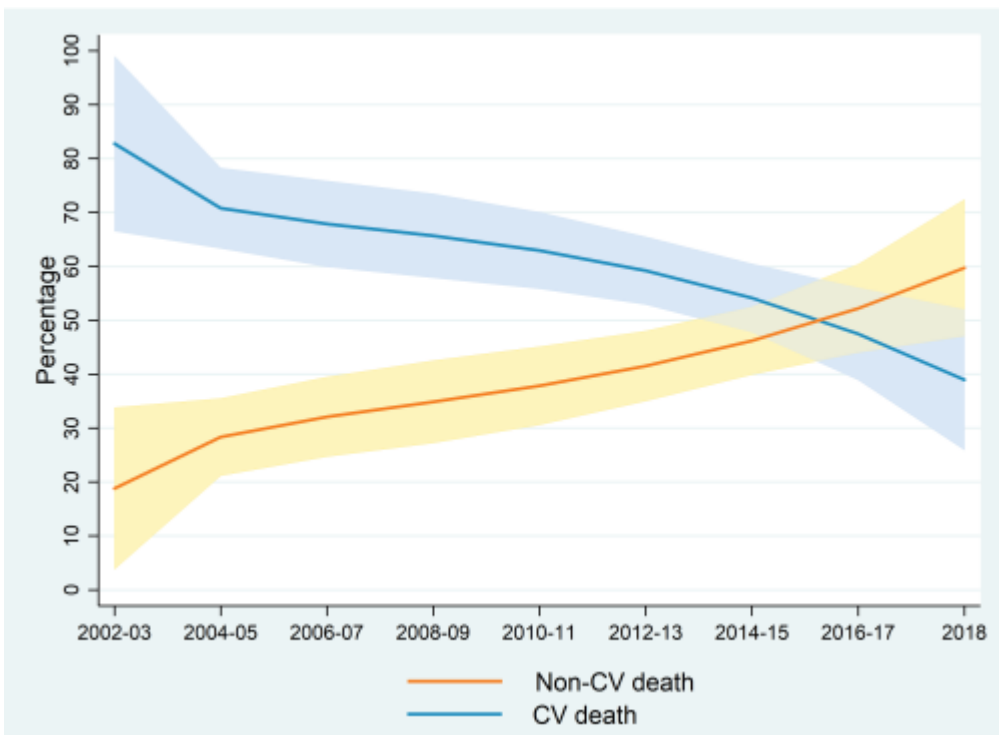
Is er een directe link?

- oncopatiënt
 - coronairlijden/hartfalen/CVA x 10
 - na genezing: CV dood x 10 tov algemene bevolking
 - "kanker is een onafhankelijke CV risicofactor"
- hartfalenpatiënt
 - kanker +24% over alle leeftijdsgroepen

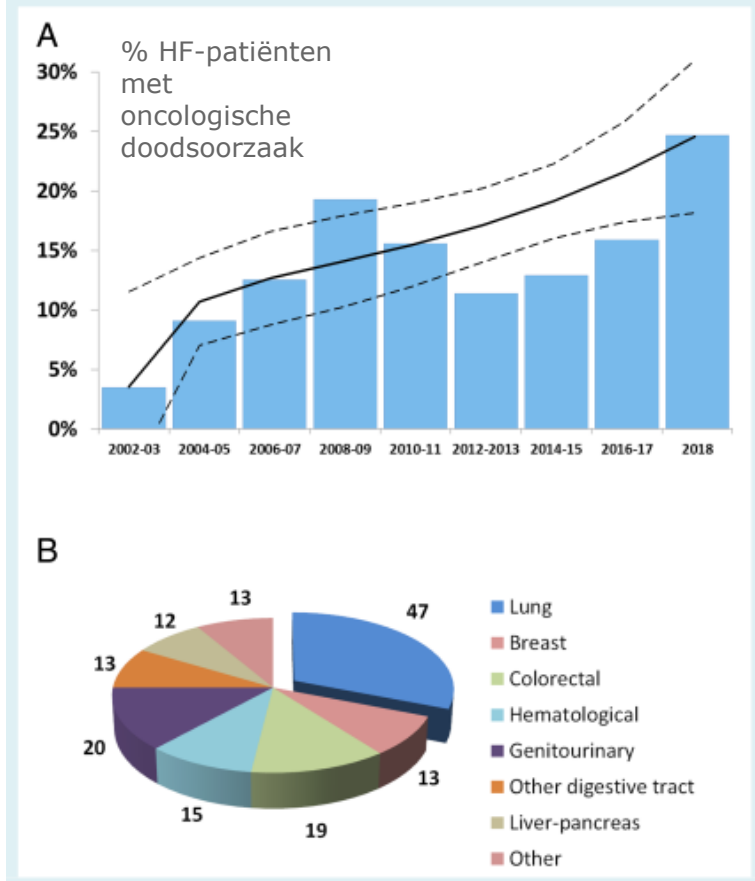


Cumulative incidence of cancer in the heart failure (HF) cohort and the background population adjusted for death from all causes.

Doodsoorzaak hartfalenpatiënt

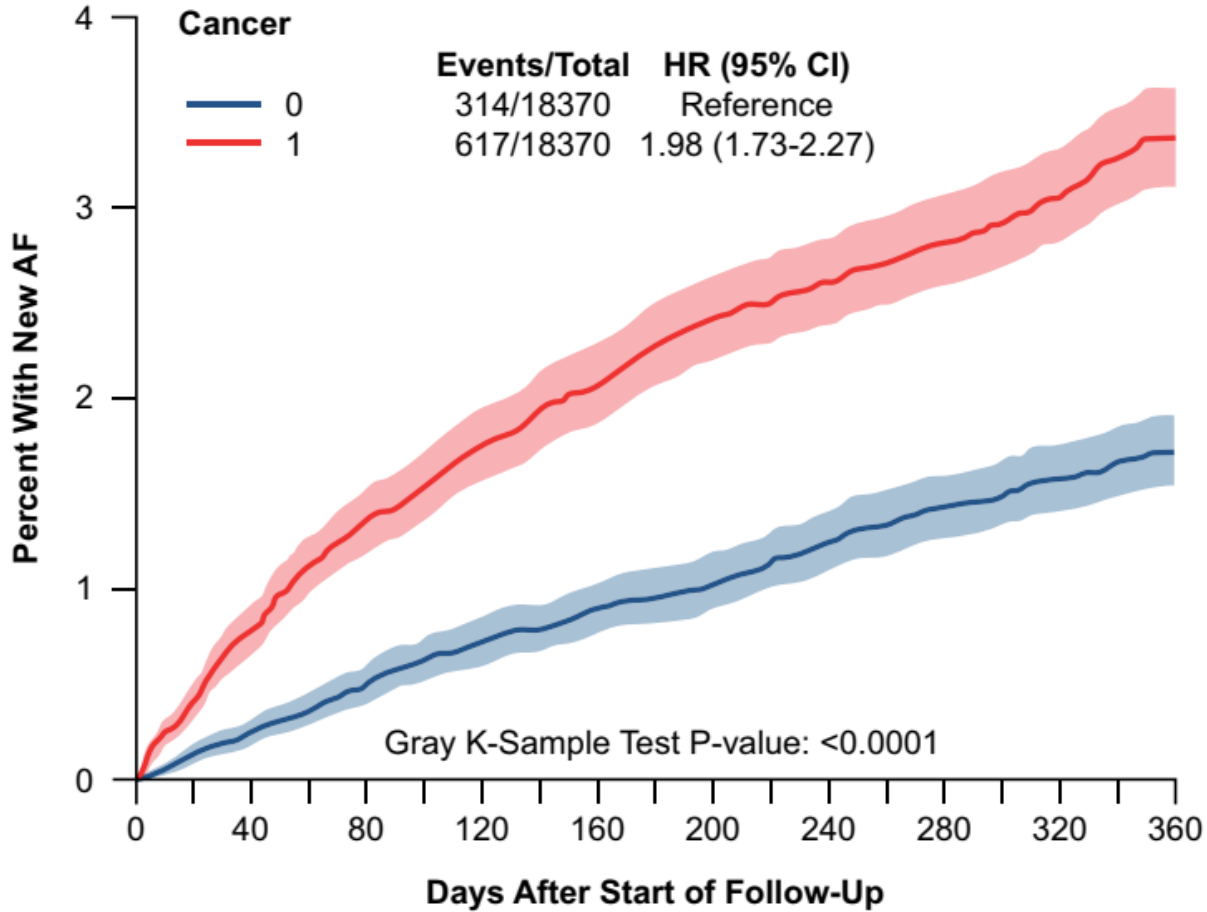


vooral kanker! →

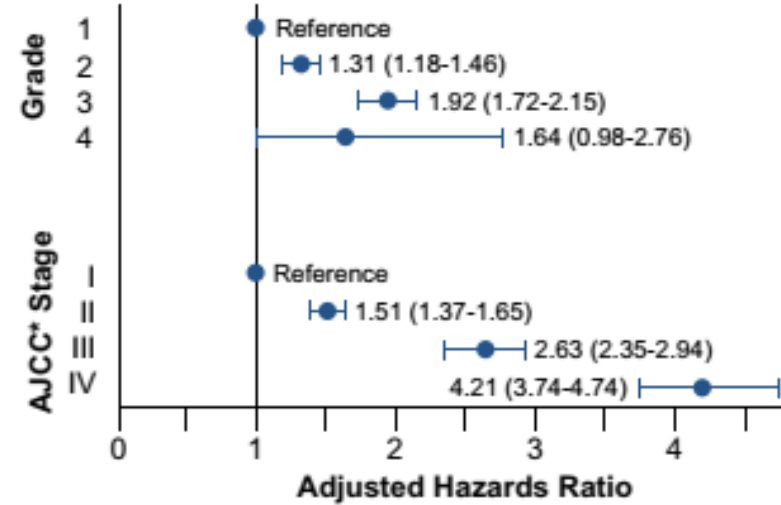


VKF bij borstkanker

Incidence of Atrial Fibrillation (AF)

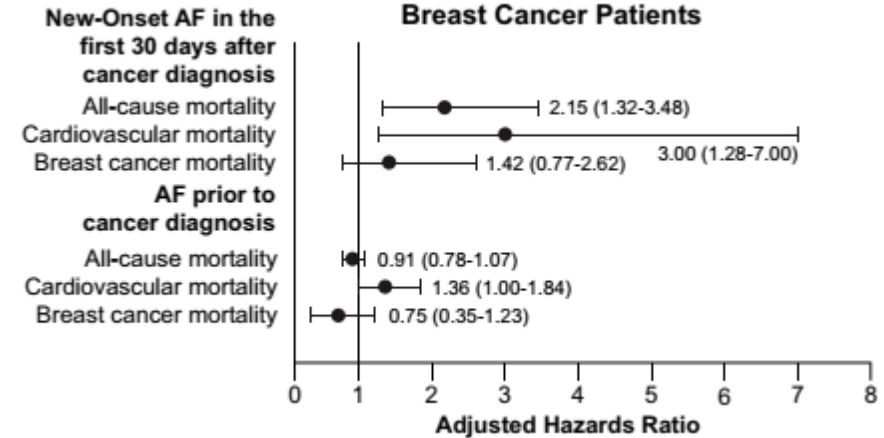


Cancer Specific Risk Factors for AF



* AJCC = American Joint Committee on Cancer

Mortality After AF in Breast Cancer Patients



doel

- ❑ preventie, vroege diagnose en behandeling van 'cardio-onco-problemen'
 - ❑ 'pre-chemo-consult'
 - optimaliseren van voorafbestaande CV aandoeningen en risicofactoren
 - opvolgingschema i.f.v. risico-inschatting

- ❑ cardiologie ten dienst van de oncologische behandeling
 - beperken van therapie-onderbrekingen
 - faciliteren van behandelingen met groter CV risico

- ❑ introduceren van systematiek om individuele beslissingen te reduceren

==> betere outcome (CV én oncologisch)

rolverdeling

- ❑ **radiotherapeut/oncoloog:**
 - ❑ actief opzoeken, selecteren en verwijzen van risicopatiënten

- ❑ **cardioloog:**
 - ❑ CV optimalisatie
 - ❑ kwalitatief hoogstaande beeldvorming
 - ❑ opvolging ifv risicostratificatie
 - ❑ vroege interventies

- ❑ **team:**
 - ❑ verderzetten, aanpassen of onderbreken van kankerbehandelingen in geval van CV problemen
 - ❑ wederzijdse educatie

- ❑ **allen (inclusief huisarts)**
 - ❑ cardiovasculaire preventie
 - ❑ (verwijzen)

Luc Akoe, 29j nieuwe diagnose borstca.



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risico-inschatting



zo sterk mogelijk
aan de start



take off



monitoring en
overleg

HET TRAJEKT



stop therapie

verdere opvolging



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waarmee het allemaal begint

BASELINE RISICO-INSCHATTING

1. A-KOZ
2. ECG
3. TTE
4. troponines: interpreteren in klinische context

Baseline clinical CV assessment, physical exam and **ECG** are recommended in all cancer patients scheduled for cardiotoxic therapies*

	Patient risk level	TTE^b	NP	cTn
Anthracyclines	Very high risk, Moderate risk, Low risk	Class I, Class IIa, Class IIb	Class I, Class IIa, Class IIb	Class I, Class IIa, Class IIb
HER2-targeted therapies ^c	Very high risk, Moderate risk, Low risk	Class I, Class IIa, Class IIb	Class I, Class IIa, Class IIb	Class I, Class IIa, Class IIb
Fluoropyrimidines	Other conditions	Class I		
VEGFi	Very high risk, Moderate risk, Low risk	Class I, Class IIa, Class IIb	Class IIa, Class IIb	
Second- and third-generation BCR-ABL TKI ^d	Other conditions	Class IIa		
BTK inhibitors	Very high risk	Class I		
PI ^e	Very high risk, Moderate risk, Low risk	Class I, Class IIa, Class IIb	Class I, Class IIa	
RAF and MEK inhibitors	Very high risk, Moderate risk, Low risk	Class I, Class IIa, Class IIb	Class IIa, Class IIb	
ICI	Very high risk, Other conditions	Class I, Class IIa, Class IIb	Class I, Class IIa, Class IIb	Class I, Class IIa, Class IIb
RT to a volume including the heart	Other conditions	Class IIa		
HSCT	Other conditions	Class I, Class IIa	Class IIa	

Very high risk
 Moderate risk
 Low risk
 Other conditions
 Class I
 Class IIa
 Class IIb

An ECG is recommended in all patients starting cancer therapy as part of their baseline CV risk assessment.

I **C**

Baseline comprehensive TTE is recommended in all patients with cancer at high risk and very high risk of CV toxicity before starting anticancer therapy.^{d,54}

I **C**

categorieën

klasse-specifiek schema

--> laag/medium/hog/zeer hoog

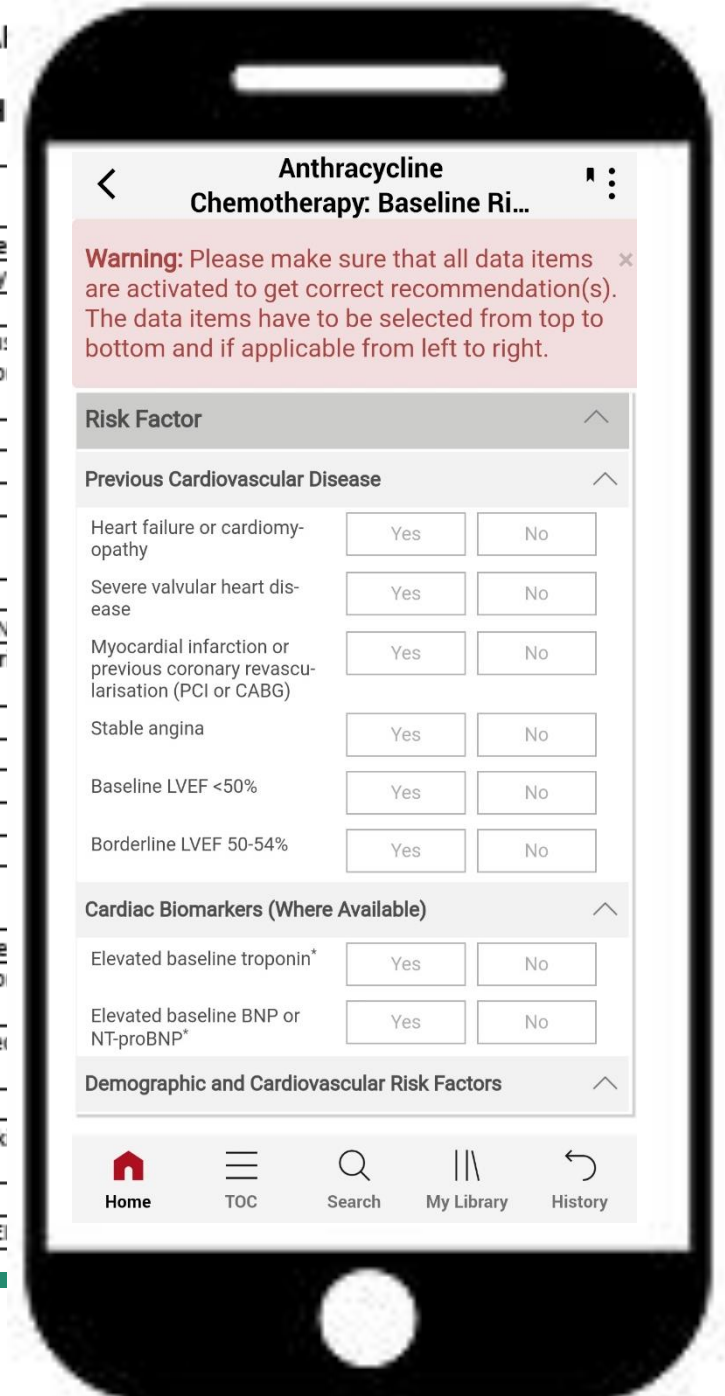
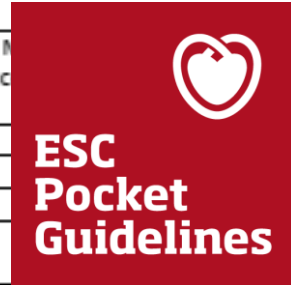
- 5 klassieke risicofactoren (AHT – chol – roken – DM – obesitas)
- CV en oncologische voorgeschiedenis
- Tn en NT-proBNP
- type behandeling

*als medium risk factors:
1 pt = laag risico
2-4 ptn = medium risico
≥5 = hoog risico*

BASELINE CAI

ANTH

Risk Factor
Previous cardiovascular disease
Heart failure or cardiomyopathy
Severe valvular heart disease
Myocardial infarction or previous coronary revascularisation (PCI or CABG)
Stable angina
Baseline LVEF <50%
Borderline LVEF 50-54%
Elevated baseline troponin*
Elevated baseline BNP or NT-proBN
Demographic and cardiovascular risk factors
Age ≥80 years
Age 65-79 years
Hypertension ⚡
Diabetes mellitus +
Chronic kidney disease ^
Previous cardiotoxic cancer treatment
Previous anthracycline exposure
Prior radiotherapy to left chest or mediastinum
Previous non-anthracycline-based chemotherapy
Lifestyle risk factors
Current smoker or significant smoking history
Obesity (BMI>30)
RISK LEVEL



categorieën

- systematisch bij **elke** patiënt met cardiotoxische behandeling
- verwijst de **hoog en zeer hoog** risico
- cardiologische 'optimalisatie' en opstellen opvolgingsplan

The screenshot shows a mobile application interface for 'Anthracycline Chemotherapy: Baseline Ri...'. At the top, there is a warning message: 'Warning: Please make sure that all data items are activated to get correct recommendation(s). The data items have to be selected from top to bottom and if applicable from left to right.' Below the warning, there are several sections for data entry:

- Risk Factor**: A section header with an expandable arrow.
- Previous Cardiovascular Disease**: A section header with an expandable arrow, containing several items with 'Yes' and 'No' buttons:
 - Heart failure or cardiomyopathy
 - Severe valvular heart disease
 - Myocardial infarction or previous coronary revascularisation (PCI or CABG)
 - Stable angina
 - Baseline LVEF <50%
 - Borderline LVEF 50-54%
- Cardiac Biomarkers (Where Available)**: A section header with an expandable arrow, containing:
 - Elevated baseline troponin*
 - Elevated baseline BNP or NT-proBNP*
- Demographic and Cardiovascular Risk Factors**: A section header with an expandable arrow.

At the bottom of the screen, there is a navigation bar with icons for Home, TOC, Search, My Library, and History.

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zo sterk mogelijk
aan de start

If you change nothing, nothing changes

PREVENTIE

Preventie

Management of CVD and CVRF according to ESC Guidelines



In patients at high and very high risk of CTRCD

huisarts + oncoloog + cardioloog



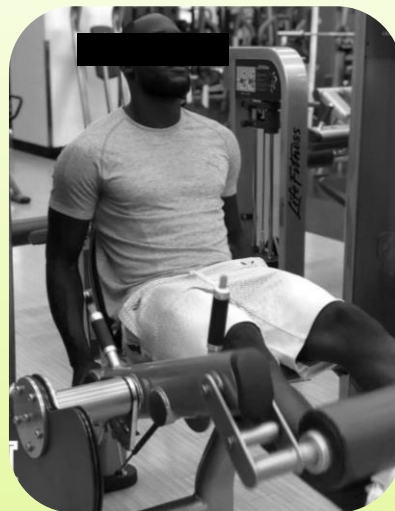
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take off

zonder uitstel

START BEHANDELING

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vergeet niet te overleggen

MONITORING

richtlijnen

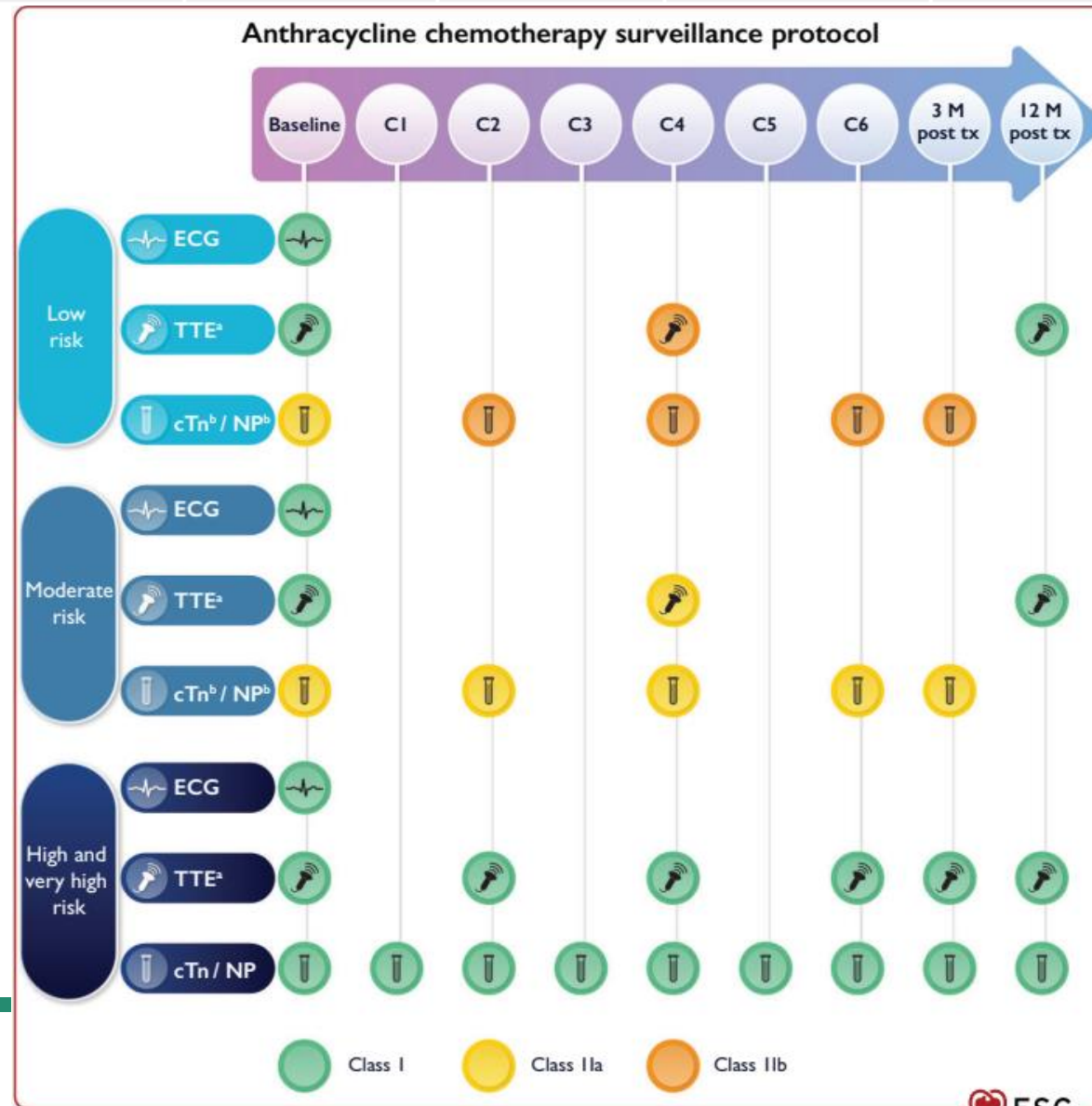
ANTHRACYCLINES

Anthracyclines

- hartfalen 3-30% (dosisgebonden)
- aritmie

Table 5 Anthracycline equivalence dose $\geq 250 \text{ mg doxorubicine/m}^2 = \text{hoog risico}$

	Doxorubicin	Epirubicin	Daunorubicin	Mitoxantrone	Idarubicin ^a
CV toxicity dose ratio	1	0.8	0.6	10.5	5
Isoequivalent dose	100 mg/m ²	125 mg/m ²	167 mg/m ²	9.5 mg/m ²	20 mg/m ²



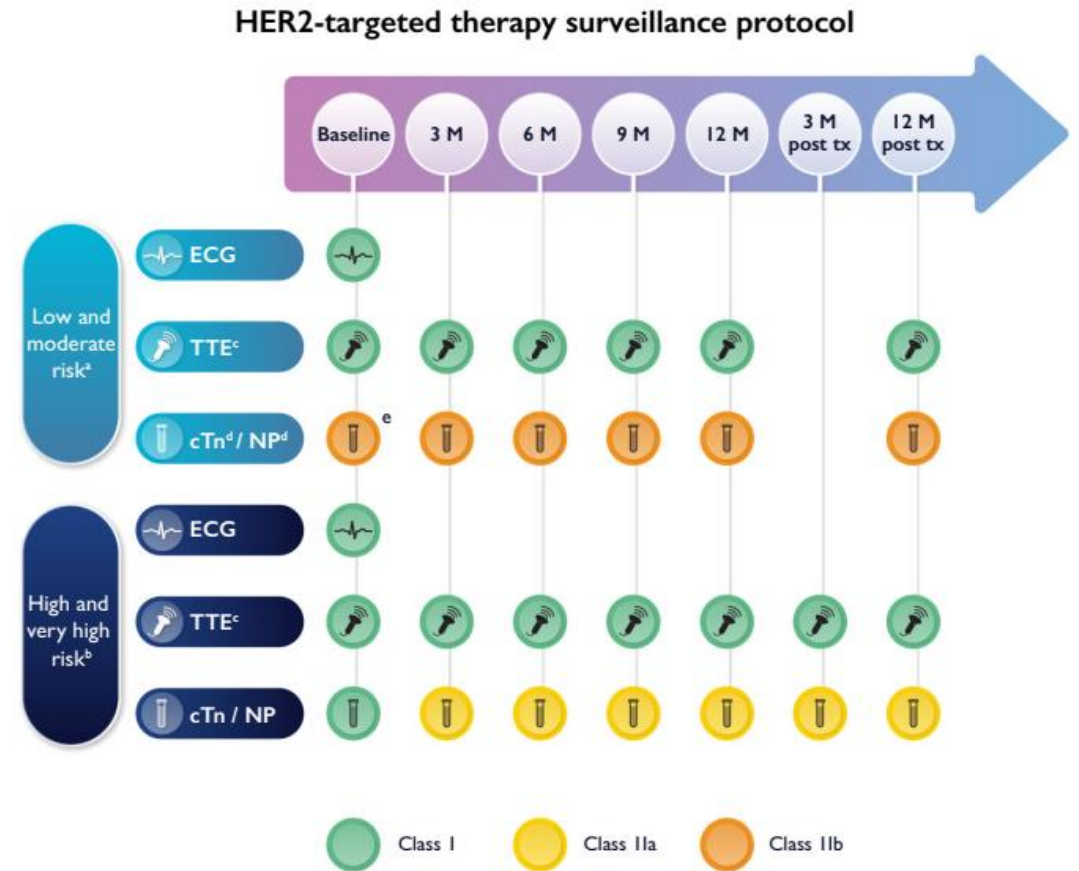
richtlijnen

ANTI-HER2

trastuzumab (Herceptine®)

trastuzumab emtansine (= T-DM1 = Kadcyła®)
pertuzumab (Perjeta®)
lapatinib (Tyverb®)
tucatinib (Tukysa®)

- hartfalen (tot 15%)
- AHT



richtlijnen

**VEGFI / BCR-ABL / PROTEASOOM-I
/ RAF-MEK / IMMUNOCHECKPUNT-
INHIBITIE ...**

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Het is wat het is

EINDE
BEHANDELING



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Soms stopt het nooit

LANGE TERMIJN



Cardiale controle jaar 1 na R/

- TTE
- Tn (en NT-proBNP) hebben hoge neg. pred. waarde
- wie opvolgen?
 - enkel als goede prognose

- (zeer) hoog baseline risico: maand 3 en 12
- ≥ 250 mg doxorubicine/m²
- RT >15 Gy Mean Heart Dose (of ≥ 35 Gy absoluut)
- ≥ 100 mg doxorubicine/m² + RT > 5Gy MHD (≥ 15 Gy)

- stamcel: ^eHigh-risk HSCT patients: allogenic HSCT; pre-existing CVD or multiple uncontrolled CVRF; cancer treatment history (mediastinal or mantle field radiation, alkylating agents, >250 mg/m² doxorubicin or equivalent); conditioning schemes (total body irradiation, alkylating agents); development of GVHD.

Lange termijn (>1j)

- dezelfde doelgroep

Patient education and CVRF optimization

TTE every 2 years in adults who are childhood and adolescent CS

LoE C

TTE at years 1, 3, and 5 after cardiotoxic cancer therapy and every 5 years thereafter in adult CS

RT als criterium: TTE 5-jaarlijks vanaf 5 jaar na R/

RT >15 Gy MHD: DSE, ... elke 5 à 10j

- (zeer) hoog baseline risico
- ≥ 250 mg doxorubicine/m²
- RT >15 Gy Mean Heart Dose (of ≥ 35 Gy absoluut)
- ≥ 100 mg doxorubicine/m² + RT > 5Gy MHD (≥ 15 Gy)
- stamcel:

^eHigh-risk HSCT patients: allogenic HSCT; pre-existing CVD or multiple uncontrolled CVRF; cancer treatment history (mediastinal or mantle field radiation, alkylating agents, >250 mg/m² doxorubicin or equivalent); conditioning schemes (total body irradiation, alkylating agents); development of GVHD.

capita selecta

VOORKAMERFIBRILLATIE







VKF en kanker

- minder data dan DVT
- geen gegevens voor LMWH!
- meta-analyse
- n = 8908
- NOAC vs VKA

















NOAC beter dan VKA

























	RR and 95% CI	P Value
Efficacy		
↓ stroke / system. emb.	0.52 (0.28–0.99)	0.04
↓ Ischemic stroke	0.63 (0.40–1.00)	0.05
↓ VTE	0.37 (0.22–0.63)	0.0003
≡ MI	0.75 (0.45–1.25)	0.26
≡ All-cause death	0.81 (0.49–1.32)	0.39
≡ Cardiovascular death	0.71 (0.45–1.10)	0.13
Safety		
↓ Major bleeding	0.73 (0.53–1.00)	0.05
≡ Major or NMCR	1.00 (0.86–1.17)	0.96
↓ Intracranial or gastrointestinal bleeding	0.65 (0.42–0.98)	0.04
≡ Any bleeding	0.93 (0.78–1.10)	0.39



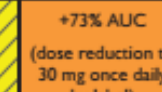






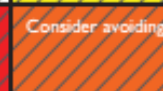
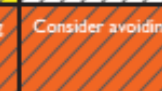
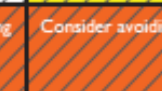
NOAC en interacties

	contraindicatie (NOAC↓)
	'caution'
	contraindicatie (NOAC↑)
	'caution'
	'consider avoiding'
	geen klinische data

	Via	Dabigatran etexilate	Apixaban	Edoxaban	Rivaroxaban
P-gp substrate		Yes	Yes	Yes	Yes
CYP3A4 substrate		No	≈25%	<4%	≈18%

Anthracyclines / Anthracenediones					
Doxorubicin	Strong P-gp induction, mild CYP3A4 inhibition; CYP3A4/P-gp competition				
Idarubicin	Mild CYP3A4 inhibition; P-gp competition				
Daunorubicin	P-gp competition; No relevant interaction anticipated				
Mitoxantrone	No relevant interaction anticipated				

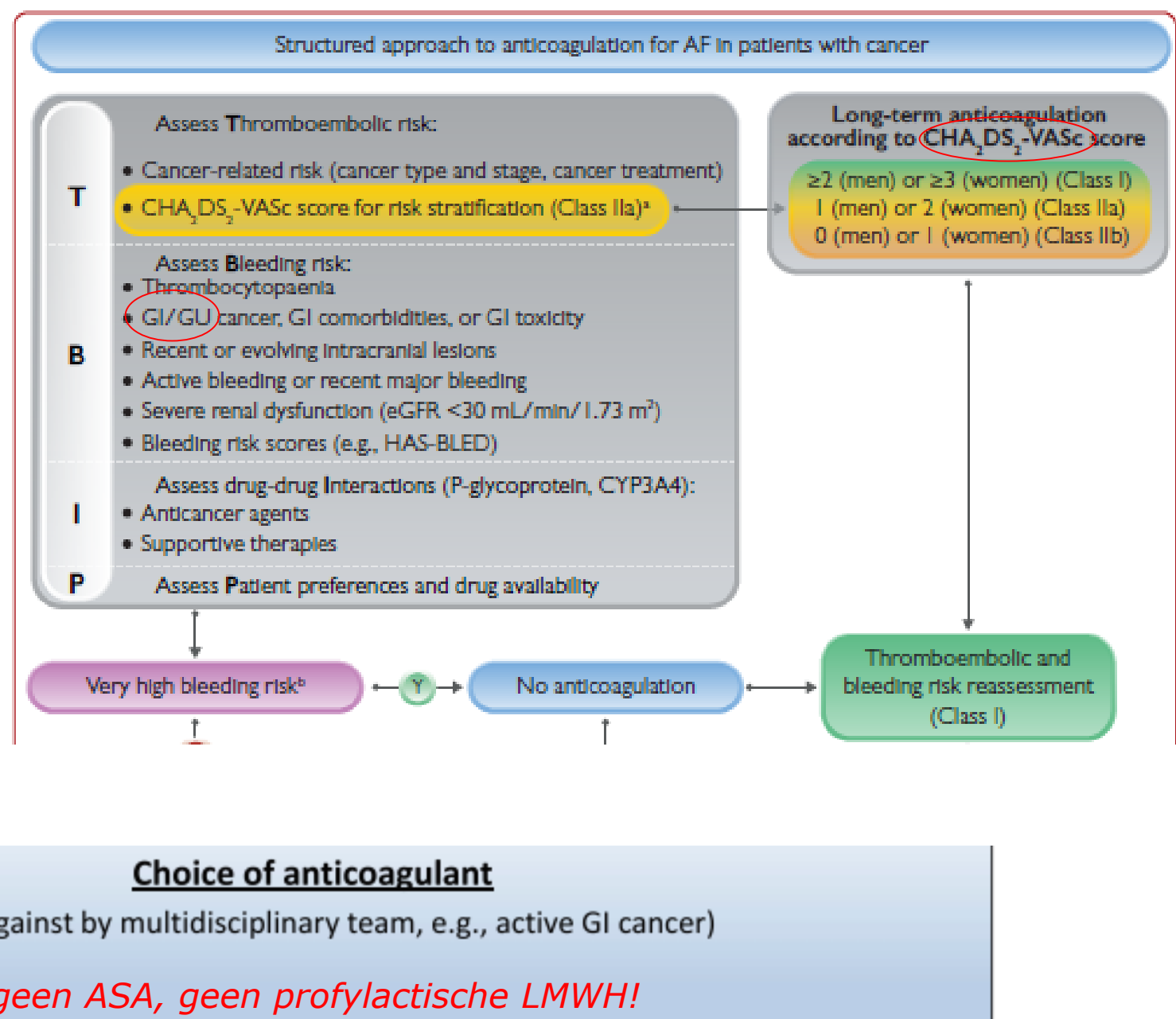
Tyrosine kinase inhibitors					
Imatinib, Crizotinib	Strong P-gp inhibition, moderate CYP3A4 inhibition; CYP3A4/P-gp competition				
Nilotinib, Lapatinib	Moderate-to-strong P-gp inhibition, mild CYP3A4 inhibition; CYP3A4/P-gp competition				
Vemurafenib	Moderate CYP3A4 induction; CYP3A4/P-gp competition				
Dasatinib	Mild CYP3A4 inhibition; CYP3A4/P-gp competition				
Vandetanib, Sunitinib	Strong P-gp inhibition; CYP3A4 competition				
Erlotinib, Gefitinib	CYP3A4 competition; no relevant interaction anticipated				

Immune-modulating agents					
Ciclosporine	Strong-to-moderate P-gp inhibition, moderate CYP3A4 inhibition; CYP3A4/P-gp competition	 SmPC	 SmPC	 +73% AUC (dose reduction to 30 mg once daily by label)	
Dexamethasone	Moderate CYP3A4 induction; CYP3A4 competition				
Tacrolimus	Strong-to-moderate P-gp inhibition, mild CYP3A4 inhibition; CYP3A4/P-gp competition	 SmPC	 Consider avoiding	 Consider avoiding	 Consider avoiding

- GEI kanker is probleem, aangezien GEI bloeding met DOAC's evenveel of méér voorkomen
- herevalueer regelmatig! (beslissing is niet ndz definitief)
- geen diltiazem of verapamil (interacties)

VKF

- geen antico bij zeer hoog bleedingsrisico:
 - hersenenmeta's
 - blpl < 25 000/ μ l
 - majeure bloeding < 1m
- “uitgelokte” VKF
 - HK, sepsis, ...
 - atriaal substraat, zelfde emboligeeen risico



Take home

- “De onco-patiënt sterft aan zijn hart”
- Risicofactoren méér in plaats van minder behandelen
 - ❖ inclusief statines
- wél: schrap andere overbodige pillen (interacties)
- Jaarlijkse opvolging van risicofactoren + lage drempel ECG ± verwijzing CAR
- Toenemend gebruik van Tn
 - ❖ niet voor spoedverwijzing
 - ❖ wel als deel van het geheel





