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Besides Heart Failure: the different forms of Cardiotossicity and Risk Factors

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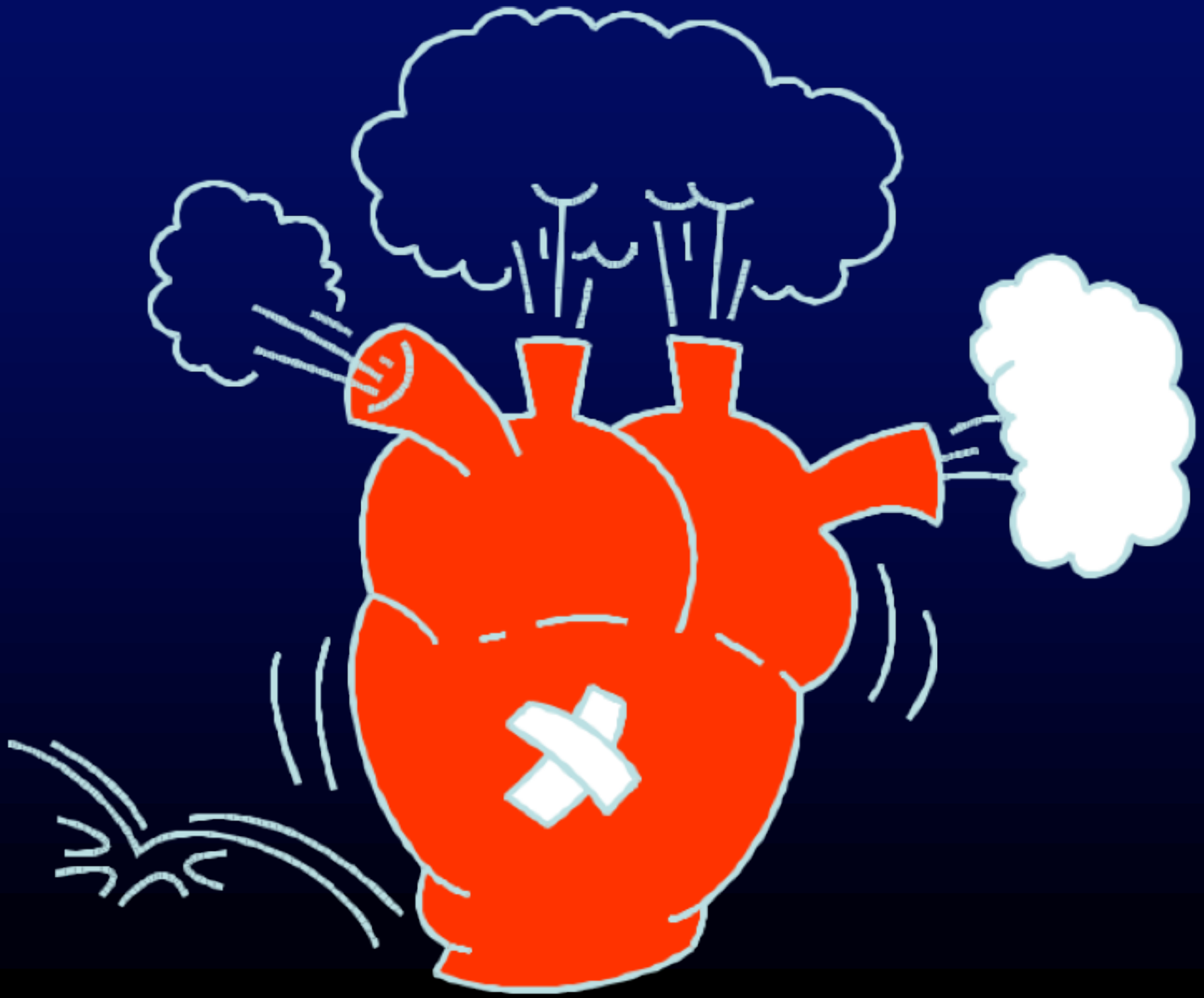
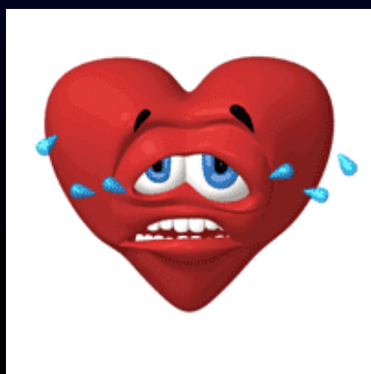
CARDIOTOSSICITÀ: quadri morfologici





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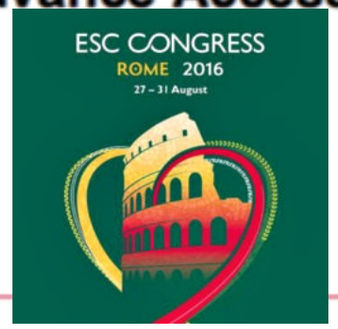

European Heart Journal
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ESC CPG POSITION PAPER

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)

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In general, the cardiovascular complications of cancer therapy can be divided into nine main categories, which are discussed in this document:

- myocardial dysfunction and heart failure (HF);
- coronary artery disease (CAD);
- valvular disease;
- arrhythmias, especially those induced by QT-prolonging drugs;
- arterial hypertension;
- thromboembolic disease;
- peripheral vascular disease and stroke;
- pulmonary hypertension and
- pericardial complications.

Non solo scompenso !

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ARRHYTHMIAS

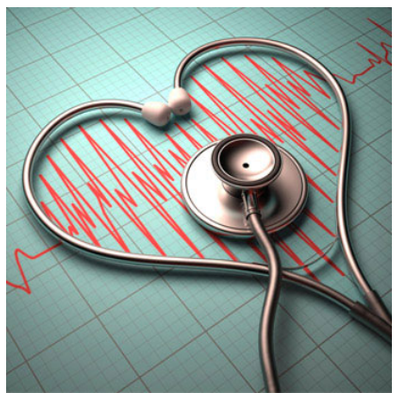

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Table 8 Cancer drug agents associated with cardiac arrhythmias

Type of arrhythmia	Causative drug
Bradycardia	Arsenic trioxide, bortezomib, capecitabine, cisplatin, cyclophosphamide, doxorubicine, epirubicine, 5-FU, ifosfamide, IL-2, methotrexate, mitoxantrone, paclitaxel, rituximab, thalidomide.
Sinus tachycardia	Anthracyclines, carmustine.
Atrioventricular block	Anthracyclines, arsenic trioxide, bortezomib, cyclophosphamide, 5-FU, mitoxantrone, rituximab, taxanes, thalidomide.
Conduction disturbances	Anthracyclines, cisplatin, 5-FU, imatinib, taxanes.
Atrial fibrillation	Alkylating agents (cisplatin, cyclophosphamide, ifosfamide, melphalan), anthracyclines, antimetabolites (capecitabine, 5-FU, gemcitabine), IL-2, interferons, rituximab, romidepsin, small molecule TKIs (ponatinib, sorafenib, sunitinib, ibrutinib), topoisomerase II inhibitors (amsacrine, etoposide), taxanes, vinca alkaloids.
Supraventricular tachycardias	Alkylating agents (cisplatin, cyclophosphamide, ifosfamide, melphalan), amsacrine, anthracyclines, antimetabolites (capecitabine, 5-FU, methotrexate), bortezomib, doxorubicin, IL-2, interferons, paclitaxel, ponatinib, romidepsin.
Ventricular tachycardia/fibrillation	Alkylating agents (cisplatin, cyclophosphamide, ifosfamide), amsacrine, antimetabolites (capecitabine, 5-FU, gemcitabine), arsenic trioxide, doxorubicin, interferons, IL-2, methothrexate, paclitaxel, proteasome inhibitors (bortezomib, carfilzomib), rituximab, romidepsin.
Sudden cardiac death	Anthracyclines (reported as very rare), arsenic trioxide (secondary to torsade de pointes), 5-FU (probably related to ischaemia and coronary spasm), interferons, nilotinib, romidepsin.

5-FU = 5-fluorouracil; IL-2 = interleukin 2; TKI = tyrosine kinase inhibitor.

Arrhythmias can be present at baseline in **16–36%** of treated patients with cancer.

ALLUNGAMENTO QTc

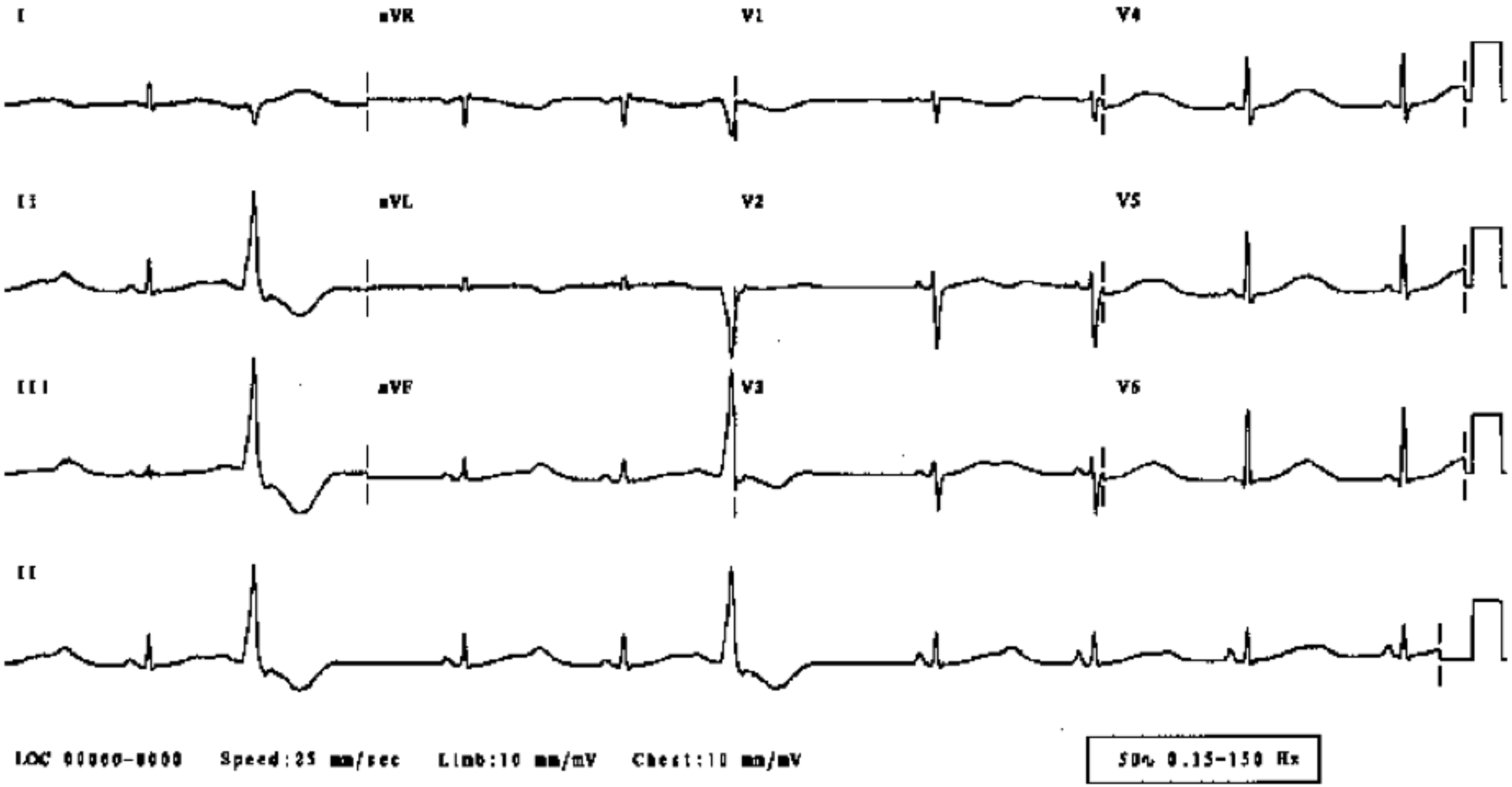


Table 10 **Risk factors for QT prolongation in cancer patients**

Risk factors for QT prolongation	
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

LQTS = long QT syndrome.

QTc normale: < 450 ms ♂, < 460 ms ♀

Gradi di tossicità (National Cancer Institute):

I : QTc > 450-470 msec

II : QTc 470-500 msec o > 60 ms rispetto al basale

III : QTc > 500 msec

IV : QTc > di 500 con segni e sintomi (TV, torsioni di punta, ipotensione, scompenso)

Table 9 Cancer drug agents associated with QT prolongation and Torsade de Pointes[151,153,154]

Cancer drug agents	Average QT prolongation (ms)	Increase in QTc >60 ms (%)	QTc >500 ms (%)	Torsade de pointes (%)
Anthracyclines				
Doxorubicin	14	11–14	NA	NA
Histone deacetylase inhibitors				
Depsipeptide	14	20–23.8	NA	NA
Vorinostat	<10	2.7–6	<1	NA
Tyrosine kinase inhibitors				
Axitinib	<10	NA	NA	NA
Bosutinib	NA	0.34	0.2	NA
Cabozantinib	10–15	NA	NA	NA
Crizotinib	9–13	3.5	1.3	NA
Dasatinib	3–13	0.6–3	<1.4	NA
Lapatinib	6–13	11	6.1	NA
Nilotinib	5–15	1.9–4.7	<1.2	NA
Pazopanib	NA	NA	2	<0.3
Ponatinib	<10	NA	NA	NA
Sorafenib	8–13	NA	NA	NA
Sunitinib	9.6–15.4	1–4	0.5	<0.1
Vandetanib	36	12–15	4.3–8	Described, % NA
Vemurafenib	13–15	1.6	1.6	Described, % NA
Others				
Arsenic trioxide	35.4	35	25–60	2.5

NA = not available.

Tabella . Farmaci potenzialmente a rischio di prolungare il tratto QT.

Farmaci Cardiovascolari	Farmaci SNC	Farmaci GI	Farmaci Antibatterici	Farmaci Antiparassitari	Farmaci Decongestionanti nasali e antistaminici
Amiodarone	Aloperidolo	Dolasetron	Azitromicina	Clorochina	Fenilefrina
Chinidina	Amitriptilina	Domperidone	Ciprofloxacina	Meflochina	Fenilpropanolamina
Disopiramide	Citalopram	Granisetron	Claritromicina	Pentamidina	Pseudoefedrina
Dobutamina	Cloralio idrato	Ondansetron	Eritromicina		Terfenadina
Dopamina	Clorpromazina		Levofloxacina		
Efedrina	Clomipramina		Moxifloxacina	**Farmaci Antimicotici**	**Altri Farmaci**
Epinefrina	Droperidolo	**Farmaci Respiratorio**	Ofloxacina		
Flecainide	Felbamato		Cotrimossazolo		
Ibutilide	Fluoxetina			Fluconazolo	Alfuzosina
Indapamide	Galantamina	Salbutamolo		Itraconazolo	Octreotide
Isradipina	Imipramina	Salmeterolo	**Farmaci Antivirali**	Ketoconazolo	Sibutramina
Midodrina	Levomepromazina	Terbutalina		Voriconazolo	Tacrolimus
Norepinefrina	Litio				Tamoxifene
Sotalolo	Metadone		Amantidina		Vardenafil
	Metilfenidato		Foscarnet		
	Nortriptilina				
	Olanzapina				
	Paroxetina				
	Quetiapina				
	Risperidone				
	Sertindolo				
	Sertralina				
	Tioridazina				
	Tizanidina				
	Trimipramina				
	Venlafaxina				

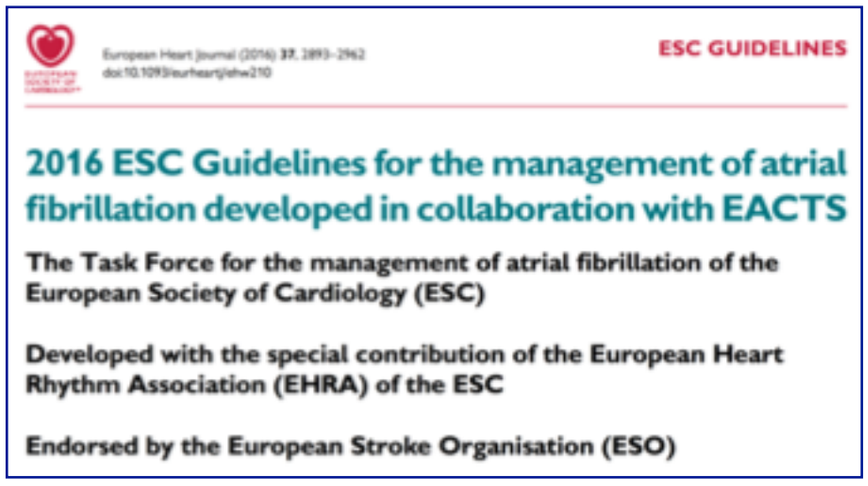
- A **12-lead ECG** should be recorded and the **QT interval**, corrected for heart rate with Bazett's or Fridericia's formula, should be obtained in **all** patients at baseline.

- Patients with a history of QT prolongation, relevant cardiac disease, treated with QT-prolonging drugs, bradycardia, thyroid dysfunction or electrolyte abnormalities should be **monitored** by repeated 12-lead ECG.

- Consider treatment **discontinuation or alternative** regimens if the QTc is **>500 ms**, QTc **prolongation is >60 ms** or **dysrhythmias** are encountered.

- Conditions known to provoke torsades de pointes, especially **hypokalaemia** and extreme bradycardia, should be avoided in patients with drug-induced QT prolongation.

- Exposure to **other QT-prolonging drugs** should be **minimized** in patients treated with potentially QT-prolonging chemotherapy.



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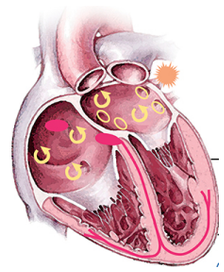
ATRIAL FIBRILLATION

- The initial approach to the **management of atrial fibrillation and atrial flutter** requires the **usual decisions** regarding rhythm management, thromboembolic prophylaxis and effective stroke prevention with oral anticoagulation

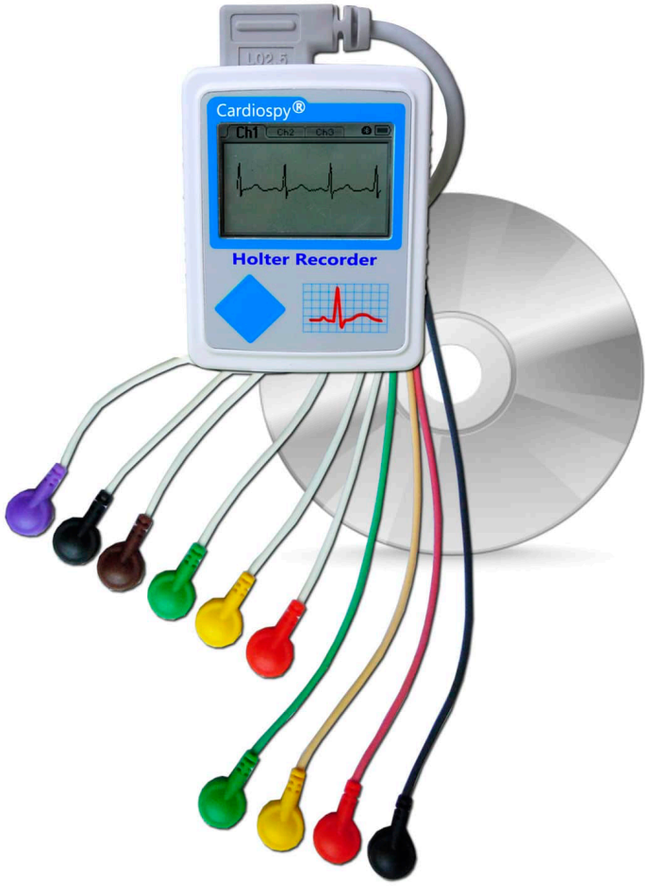
- The **balance** between **thromboembolic and bleeding risks** of atrial fibrillationis particularly **challenging** in patients with cancer. While cancer may cause a prothrombotic state, it may also predispose to bleeding. On the other hand, the CHA2DS2-VASc and HAS-BLED risk scores have **not been validated** in patients with cancer

- In patients with a **CHA_2DS_2-VASc score ≥ 2**, anticoagulation can generally be considered if the **platelet count is >50 000/mm^3**

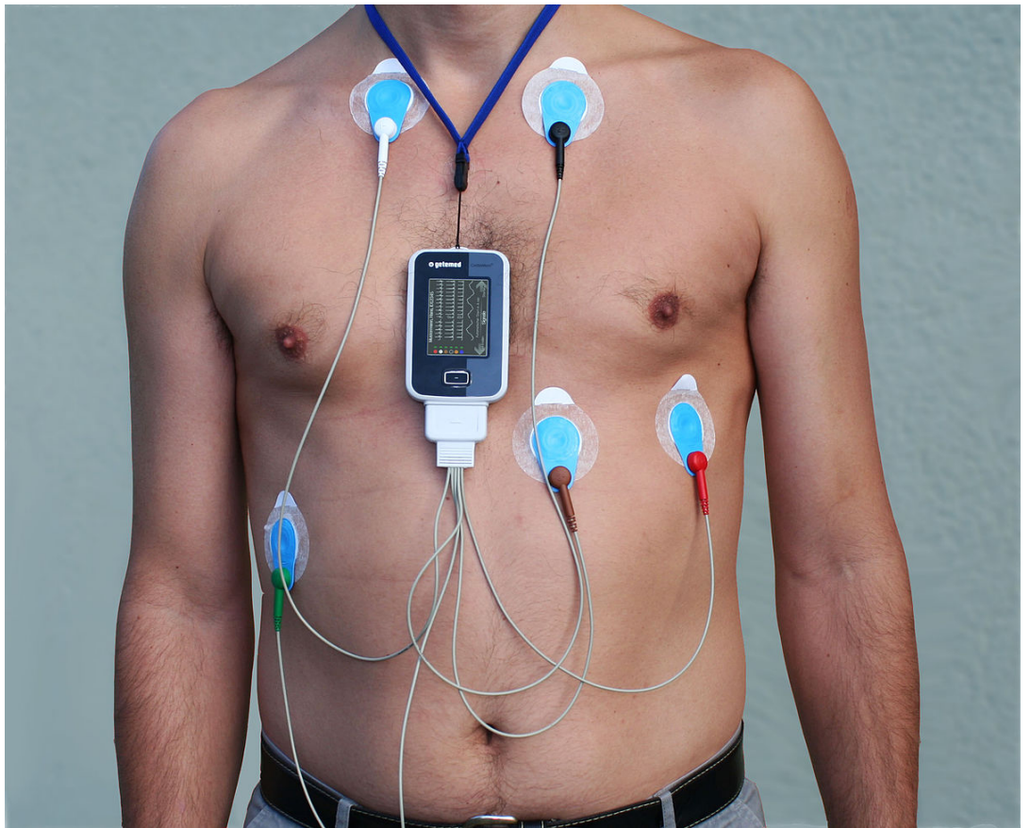


Recommendations for screening for atrial fibrillation

Recommendations	Class[a]	Level[b]	Ref[c]
Opportunistic screening for AF is recommended by pulse taking or ECG rhythm strip in patients >65 years of age.	I	B	130, 134, 155
In patients with TIA or ischaemic stroke, screening for AF is recommended by short-term ECG recording followed by continuous ECG monitoring for at least 72 hours.	I	B	27, 127
It is recommended to interrogate pacemakers and ICDs on a regular basis for atrial high rate episodes (AHRE). Patients with AHRE should undergo further ECG monitoring to document AF before initiating AF therapy.	I	B	141, 156
In stroke patients, additional ECG monitoring by long-term non-invasive ECG monitors or implanted loop recorders should be considered to document silent atrial fibrillation.	IIa	B	18, 128
Systematic ECG screening may be considered to detect AF in patients aged >75 years, or those at high stroke risk.	IIb	B	130, 135, 157



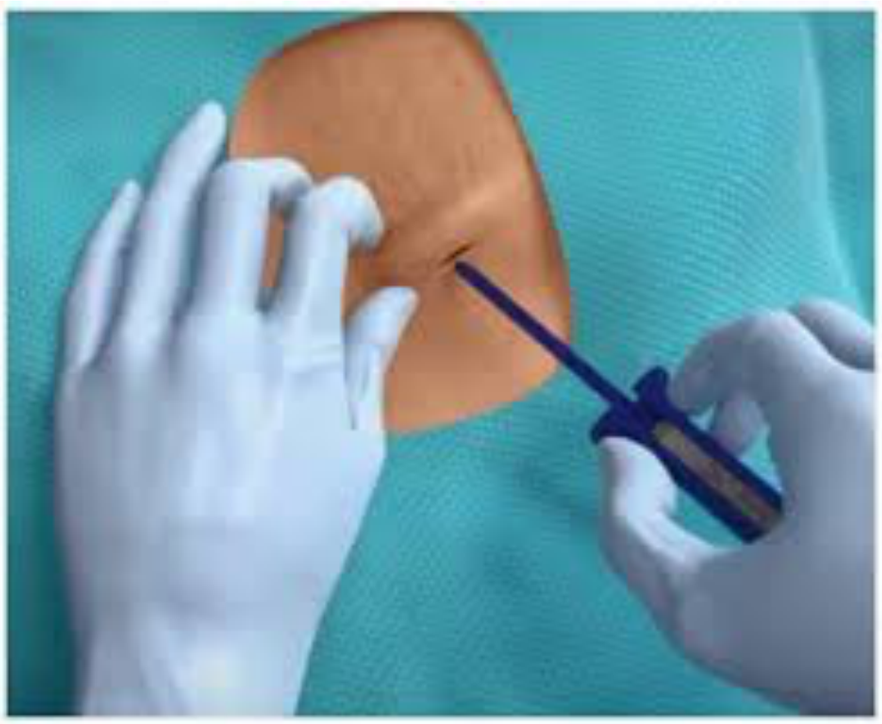
ECG HOLTER

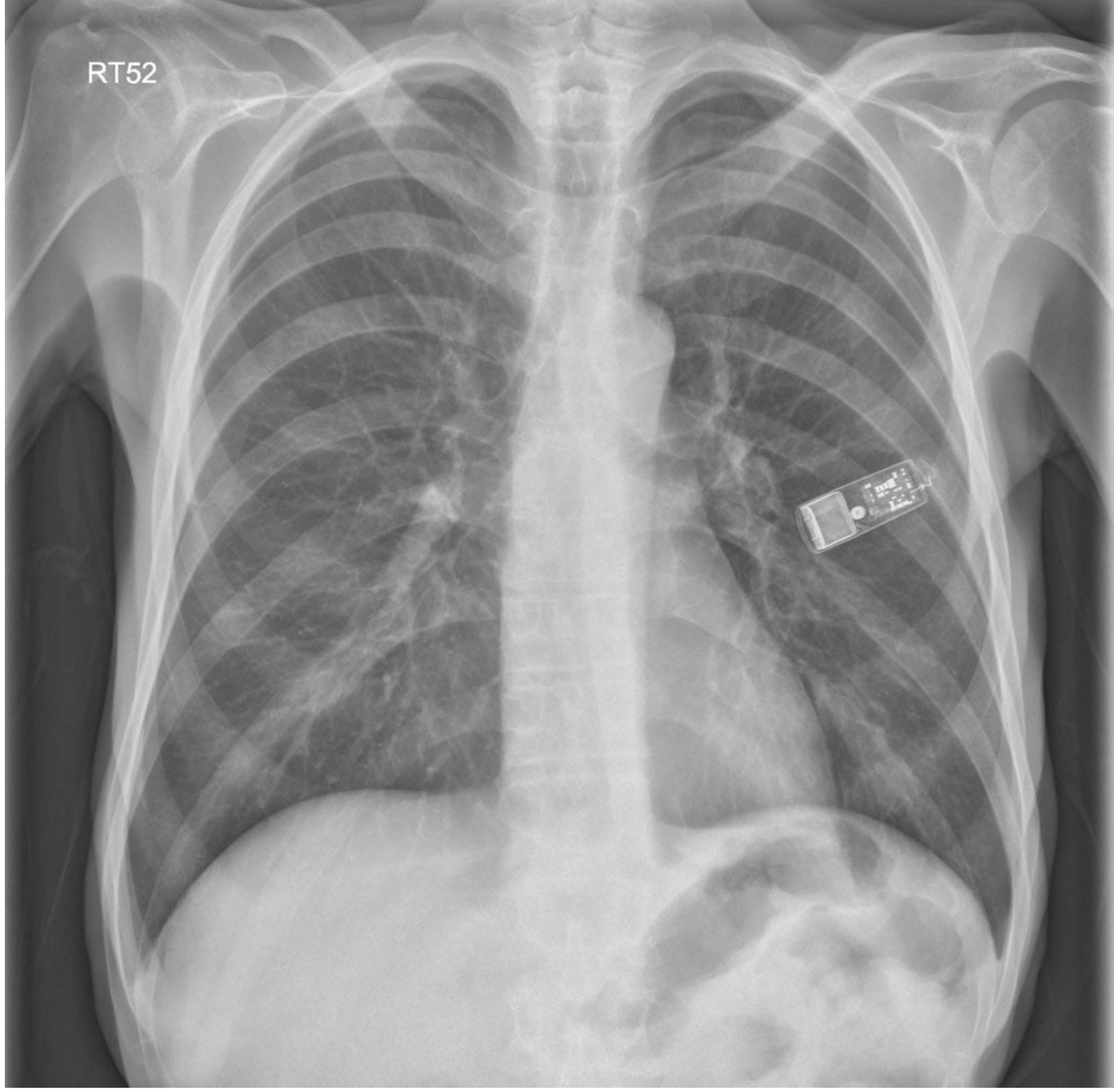


45x7x4mm

62x19x8mm

56x19x8mm





LOOP RECORDER

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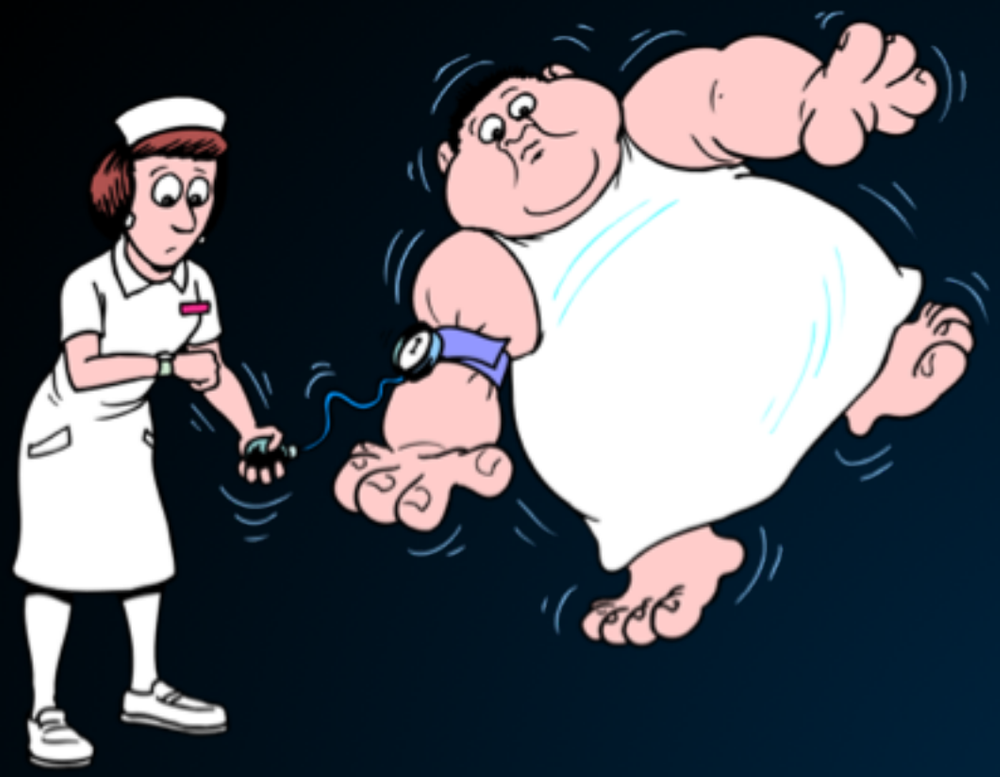
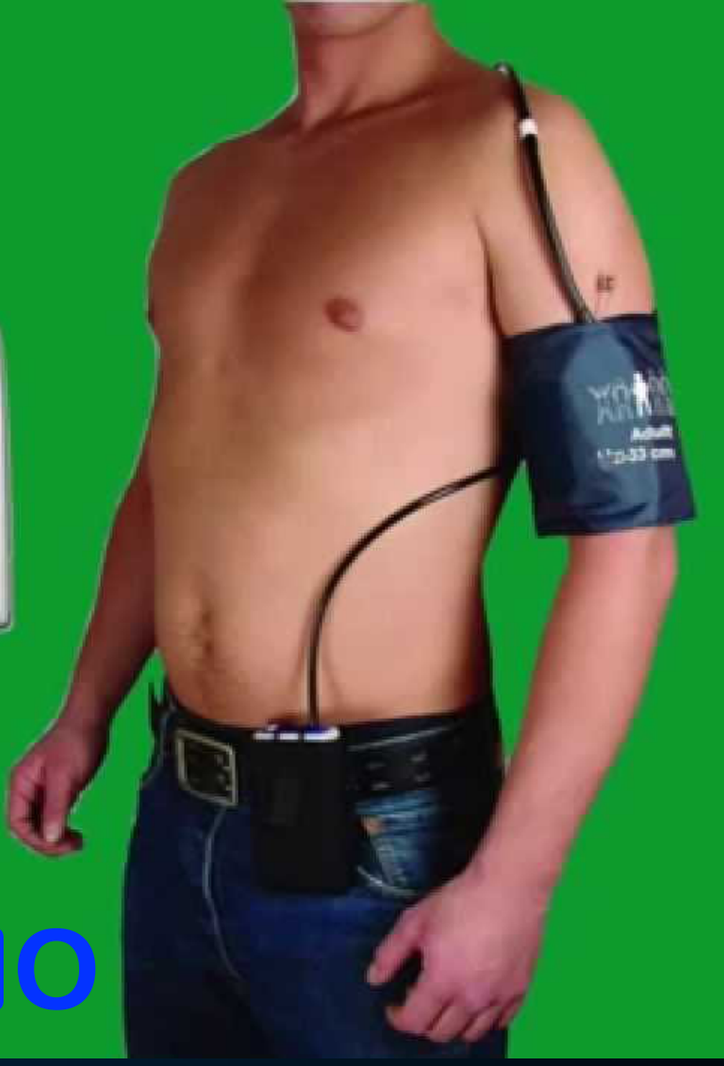
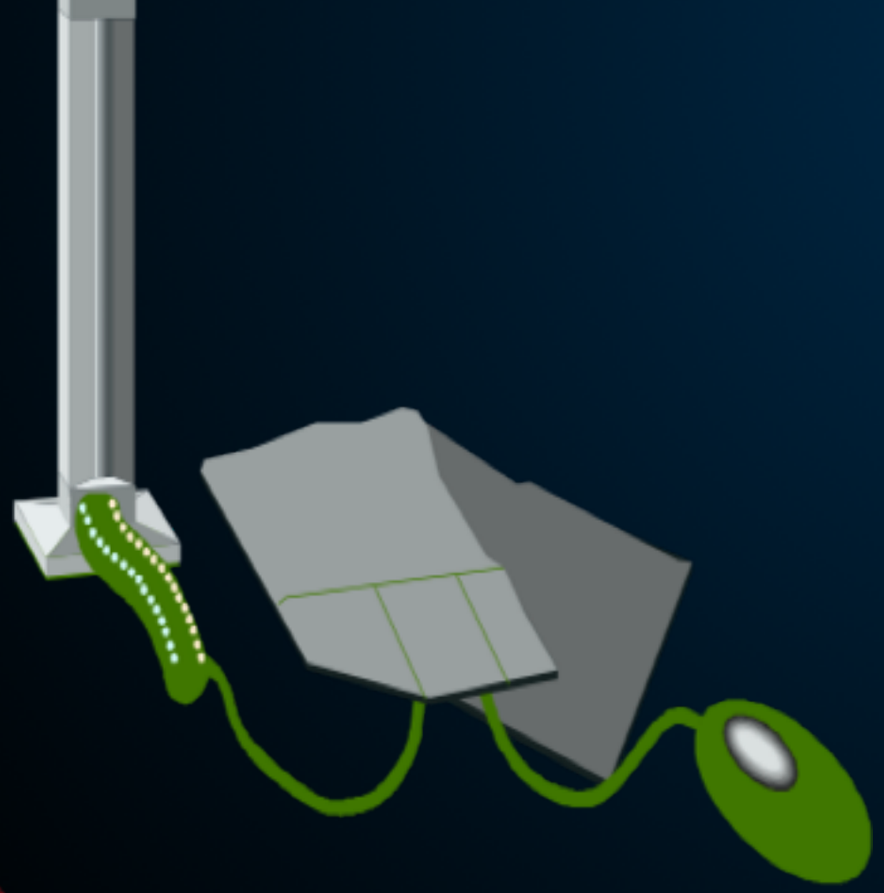
HYPERTENSION





HOLTER PRESSORIO



< 140/90 mmHg

(Ideale:< 130/80 mmHg)

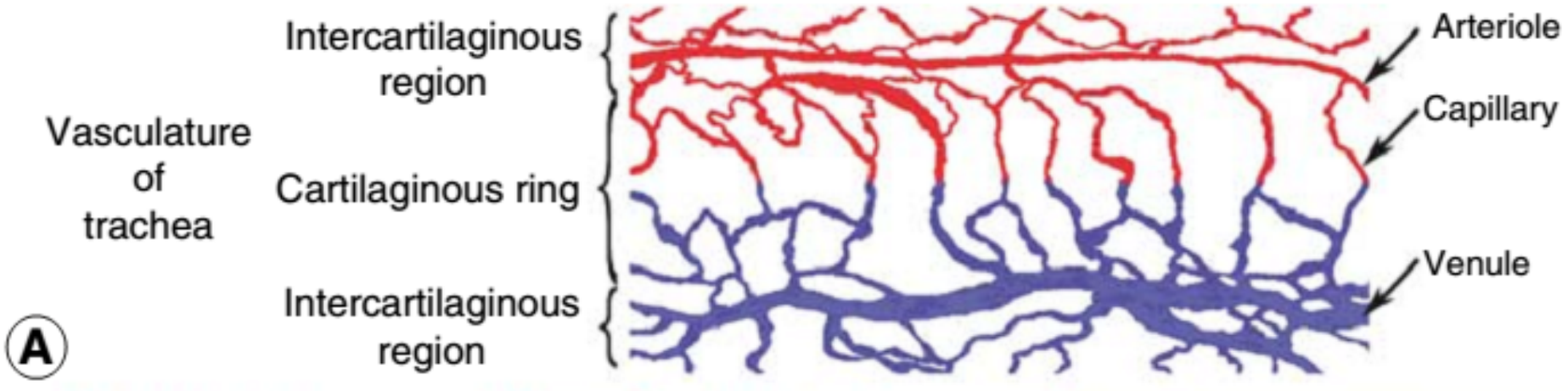
Supplementary Table **Most recent reviews and meta-analyses on the incidence of hypertension with major VEGF inhibitor treatment**

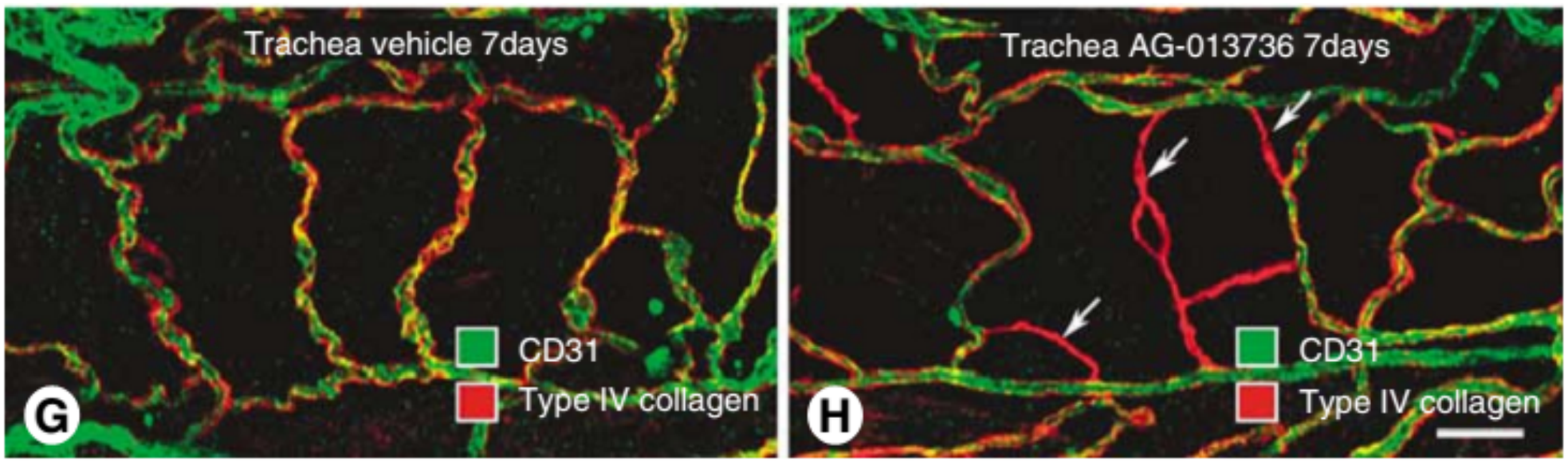
Drug	Number of studies included	Number of patients	Incidence of all grades of HTN, %	Incidence of stage 3-4 HTN, %
Bevacizumab[165]	20	6754	23.6	7.9
Sunitinib[167]	13	4999	21.6	6.8
Sorafenib[168]	13	2492	15.3	4.4
Axitinib[169]	10	1908	40.1	13.1
Vandetanib[170]	11	3154	24.2	6.8
Regorafenib[171]	5	750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

HTN = hypertension; VEGF = vascular endothelial growth factor.

Meccanismo d’azione

Danno vascolare

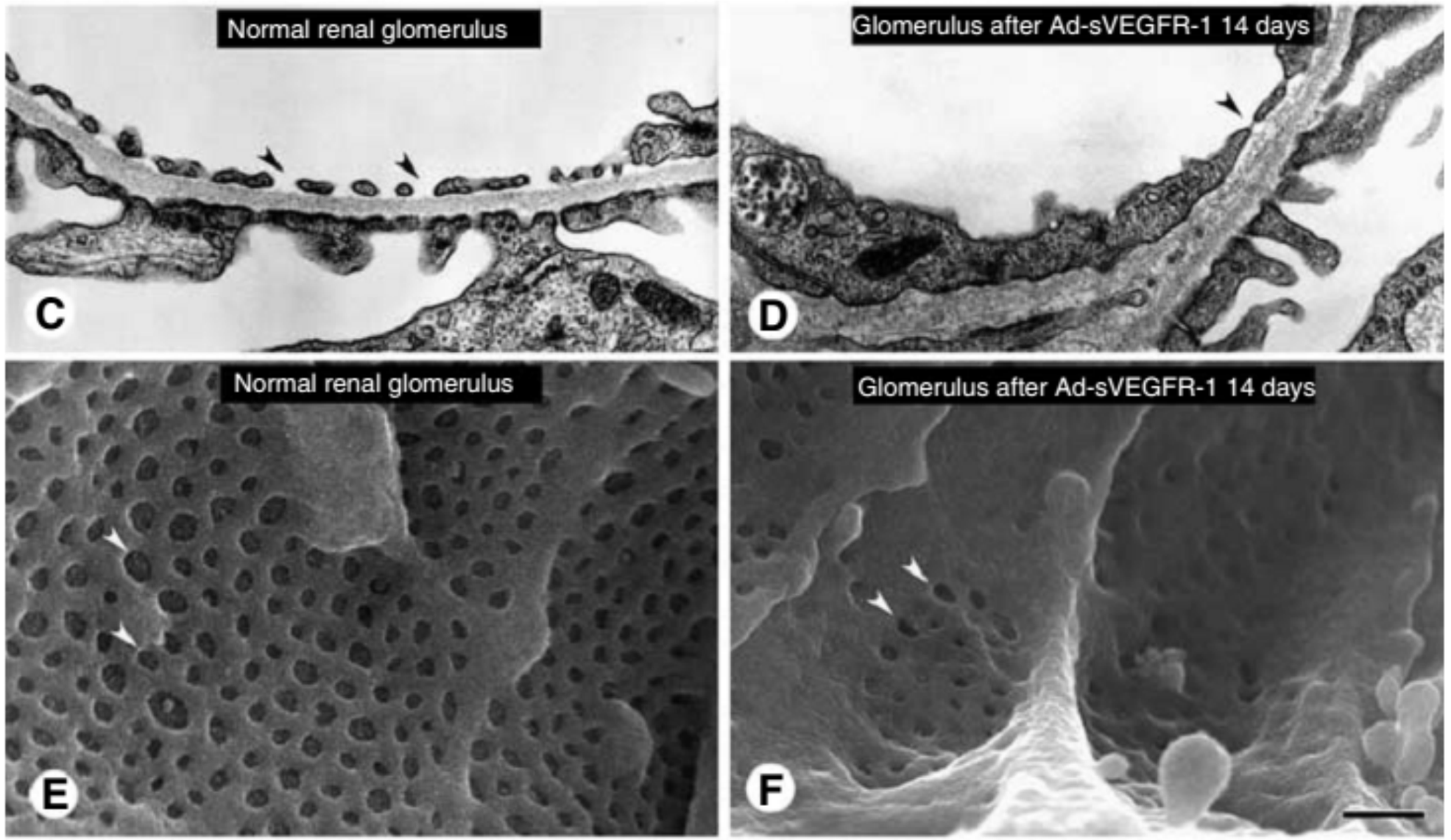




Kamba et al Br J of Cancer 2007

Meccanismo d’azione

Danno renale



Kamba et al Br J of Cancer 2007

- Hypertension should be **adequately treated according to the current standing clinical practice guidelines**, and blood pressure should be monitored **before** initiating cancer treatment and **periodically during** treatment, depending on the patient's characteristics and adequate blood pressure control (<140/90 mmHg or lower in case of proteinuria).

- Hypertension in Pts with cancer is manageable with conventional antihypertensive treatment, but **early and aggressive treatment is encouraged** to prevent the development of cardiovascular complications.

- **ACEi** or **ARBs**, **beta-blockers** and **dihydropyridine calcium channel blockers** are the preferred antihypertensive drugs.

- **Non-dihydropyridine** (Verapamil, Diltiazem) calcium channel blockers should preferably be **avoided** due to drug interactions (*CYP3A4*)

- **Dose reduction** and reinforcement of antihypertensive treatment or **discontinuation** of **VEGF inhibitors** can be considered if blood pressure is not controlled. Once blood pressure control is achieved, VEGF inhibitors can be restarted to achieve maximum cancer efficacy.

Trattamento dell'ipertensione in pazienti in terapia con anti VEGF

Target pressorio

<140/90 → si → **Stop**

no ↓ no

FdR Cardiov → es. DM, CAD, CHF, fumo, dislipidemia → **Ecocardio**

C **Calcioantagonisti**

Es.
- Amlodipina (5-10 mg)
- Felodipina (5-10 mg)
- Manidipina (10-20 mg)

Potenza / Eff.collat.

Buona maneggevolezza

Eff.collat.: tachicardia, edemi declivi

e/o

A **RAAS inibitori**

ACE-I

Ramipril (2.5-10 mg)

Antagonisti recettoriali dell'ang II

Telmisartan 20-80 mg, Valsartan 80-320 mg, Candesartan 4-32 mg, Irbesartan 150-300 mg, Losartan 12.5-100 mg

Eff.collat.: tosse Controind.: GFR<30 cc/m
Controllo periodico di Creatinina Na+ K+

Eventualmente associati a

B **Beta bloccanti**

Es. Nebivololo a dosaggi crescenti 2.5 mg aumentabile a 5 mg dopo 15 gg

Eff.collat.: bradicardia
Controind.: bradicardia, asma (relativa)

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THROMBOEMBOLIC DISEASE

Table 11 Clinical factors associated with increased risk of cancer-associated venous thromboembolism (modified from Khorana et al.[182])

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

- **Tumour cells can trigger coagulation through different pathways**, including procoagulant, antifibrinolytic and pro-aggregating activities, release of pro-inflammatory and pro-angiogenic cytokines and interaction with vascular and blood cells through adhesion molecules
- Venous thrombosis and VTE occur frequently in patients with cancer, may affect up to 20% of hospitalized patients
- Antithrombotic prophylaxis should be given for a minimum of 4 weeks after surgery
- The **detection of thrombotic events** in patients undergoing chemotherapy is based mainly on **clinical symptoms**. **No systematic screening strategy has shown any benefit**
- The decision to administer anticoagulation for VTE prevention in patients with cancer should always take into consideration the patient's **bleeding risk and life expectancy**
- **Treatment** of a confirmed episode of acute VTE in haemodynamically stable patients consists of **LMWH** given over a period of **3–6 months**. This strategy is **superior to VKA** therapy in patients with cancer in terms of reduced VTE events, with no difference regarding mortality or bleeding in clinical trials.
- **DOACs? Edoxaban** and **rivaroxaban**

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PERIPHERAL VASCULAR DISEASE AND STROKE

- Can occur (in **up to 30%**) in patients treated with **nilotinib, ponatinib or BCR-ABL TKIs** used for chronic **myeloid leukaemia**, even in the absence of CVD risk factors

- PAD can occur as **early** as in the first months of therapy or as a **late effect** several years after treatment. Other cancer therapy–related peripheral arterial toxicity includes **Raynaud's** phenomenon and ischaemic stroke (i.e. with L-asparaginase, cisplatin, methotrexate, 5-FU and paclitaxel)

- The risk of **stroke** is increased—**at least doubled**—after mediastinal, cervical or cranial **radiotherapy**.

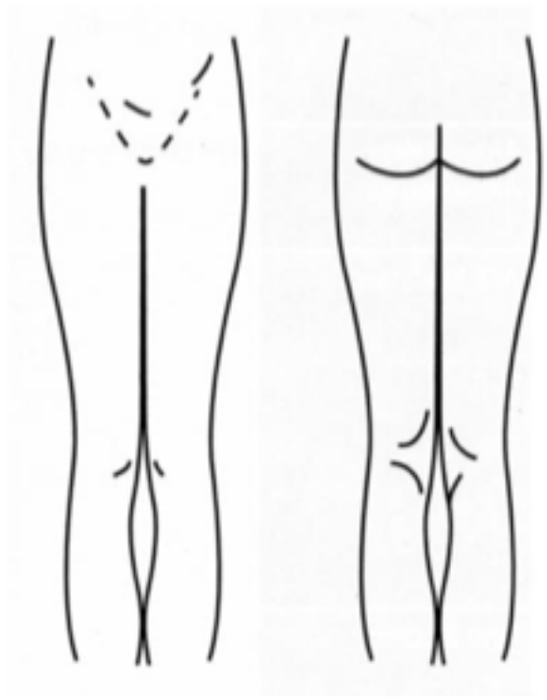
- The **assessment of PAD risk at baseline** (risk factor assessment, clinical examination, ankle–brachial index measurement) is recommended.

- **Antiplatelet drugs** should be considered mostly in **symptomatic** PAD.

Edinburgh Claudication Questionnaire

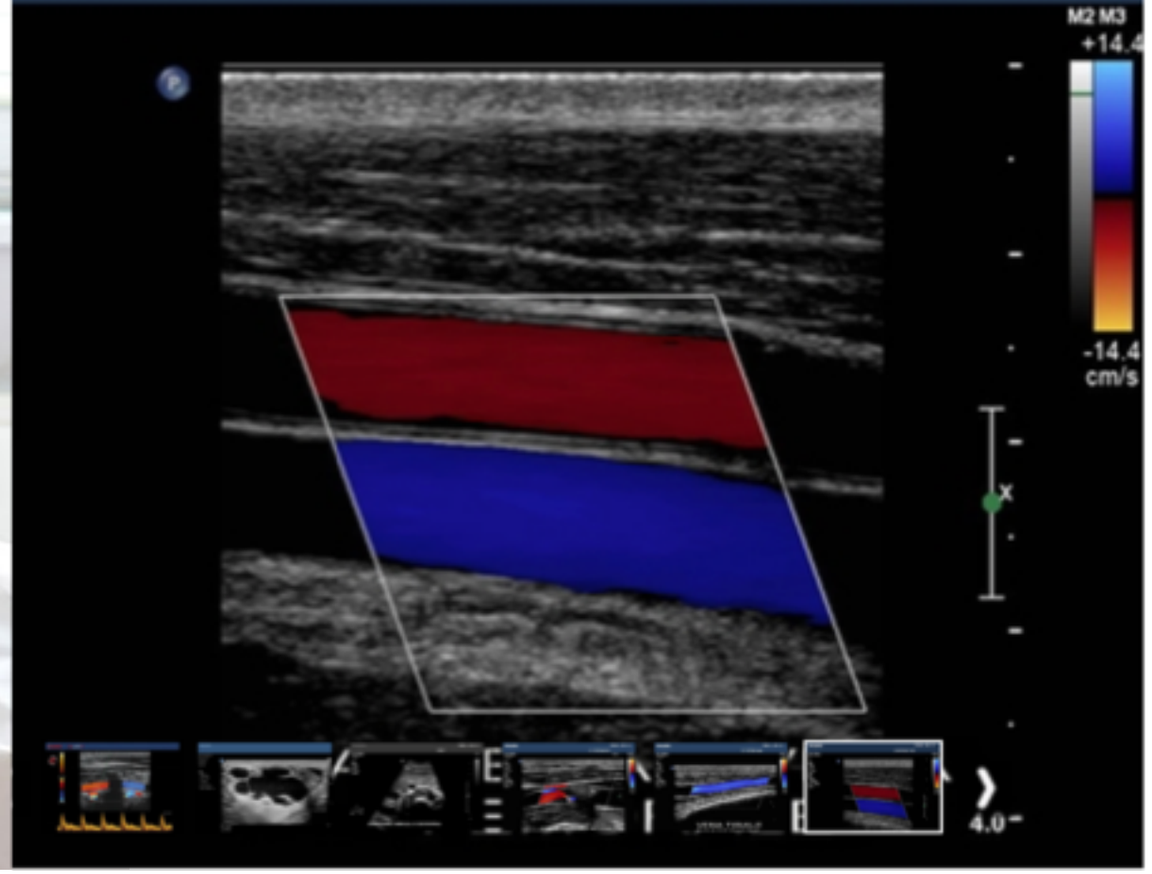
The Edinburgh Claudication Questionnaire:
CAD/PVD

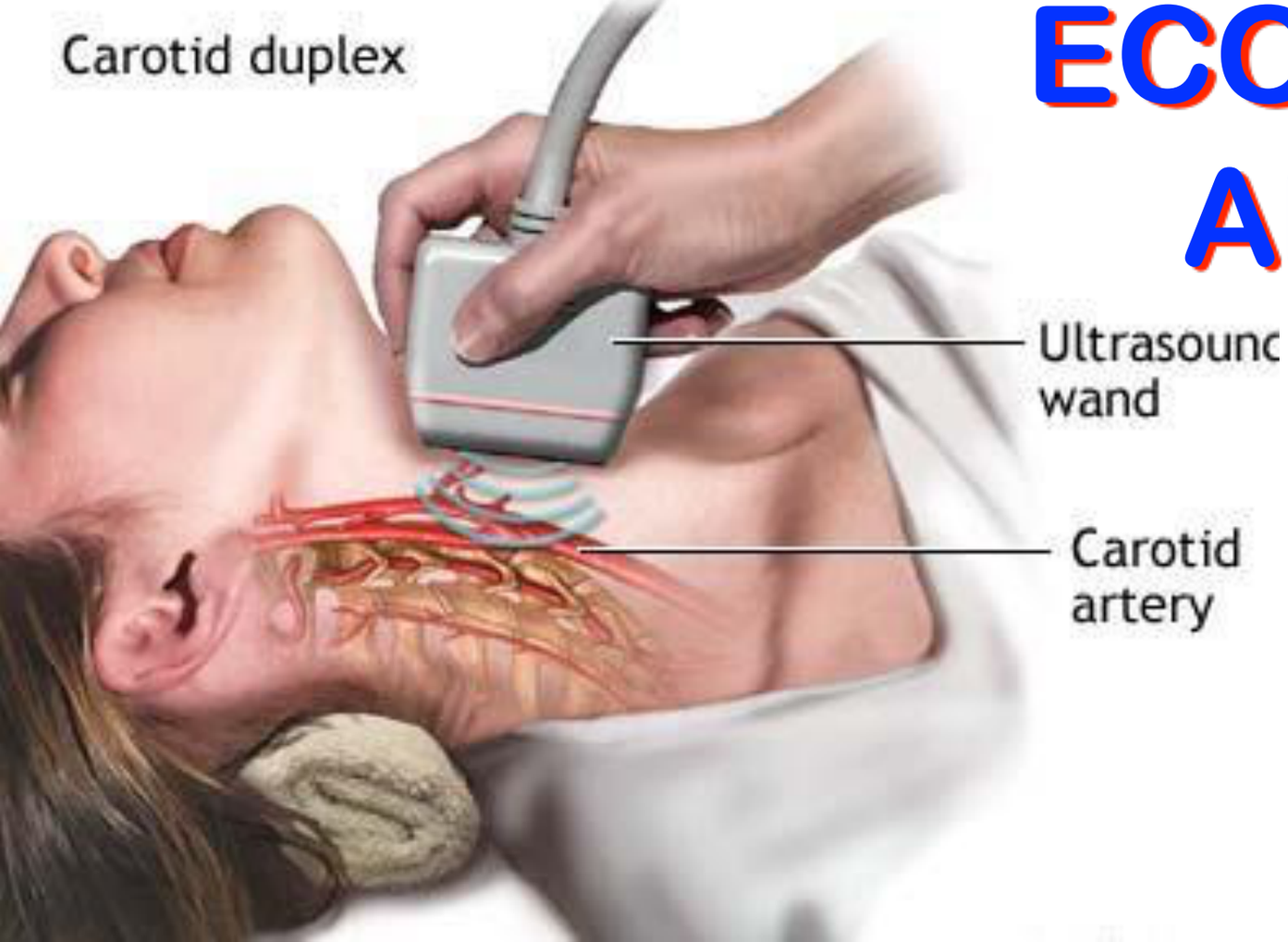
* A positive questionnaire diagnosis of claudication is made only if the ***"correct"*** answer is given to ***all questions***

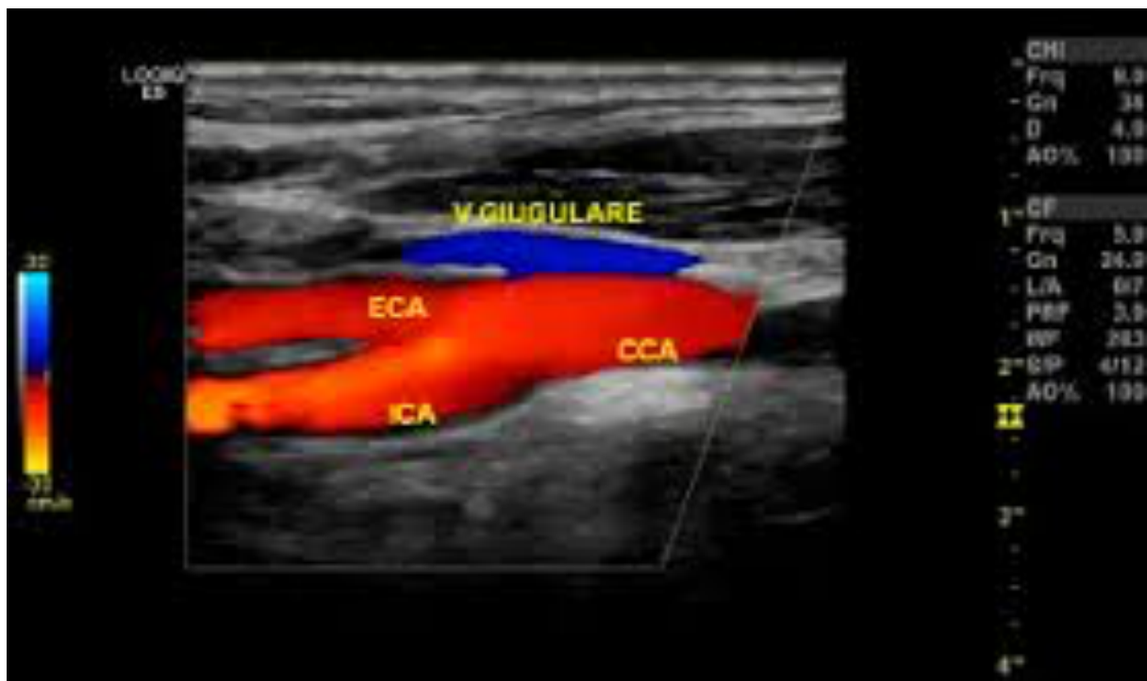
Questions	Correct Answer	
1. Do you get pain or discomfort in your legs(s) when you walk? ○ Yes ○ No ○ Unable to walk • If you answered "yes" to question 1, please answer the following questions	Yes	
2. Does the pain ever begin when you are standing or sitting still?	No	
3. Do you get it when you walk uphill or in a hurry?	Yes	
4. Do you get it when you walk at an ordinary pace on the level?	Yes	
5. What happens if you stand still? • Usually continues for more than 10 minutes? • Usually disappears in 10 minutes or less?	 No Yes	
6. Where do you get this pain or discomfort? • Mark the places with an "X" on the diagram		

Leng G et al., J Clin Epidemiol 1992; 45: 1101-1109.

ECODOPPLER TSA + ARTI INFERIORI







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PULMONARY HYPERTENSION

Pulmonary hypertension is a rare but serious complication of some cancer agents and stem cell bone marrow transplantation (**TKIs family**: imatinib, dasatinib)

Dasatinib, used as second-line treatment for chronic myelogenous leukaemia, can induce severe precapillary pulmonary hypertension.

This condition appears **8–40 months after exposure** to dasatinib, with clinical and haemodynamic presentation suggestive of PAH.

Unlike other forms of PAH, this is **often reversible** after drug discontinuation or replacement with another TKI, such as nilotinib.

Recently, **cyclophosphamide** and other alkylating agents were suggested as contributing to the development of pulmonary veno-occlusive disease

Table 12 **Strategies for surveillance and management of drug-induced pulmonary hypertension**

Baseline assessment	• Consider risk factors and associated conditions for PAH[a] • Assess NYHA/WHO functional class • Consider 6-minute walk test • Consider NT-proBNP • Assess echocardiographic level of probability of PH
Surveillance strategy	**Asymptomatic** • Assess NYHA/WHO functional class every 3 months • Assess echocardiographic level of PAP every 3 months • Consider presence of other indications for right heart catheterization • Consider further evaluation for suspected PH[a] **Symptomatic** • Assess NYHA/WHO functional class • Perform 6-minute walk test • Sample blood for NT-proBNP • Assess echocardiographic level of probability of PH • Consider indications for right heart catheterization in PH referral centre[a] • Consider interruption of cancer therapy[b]

NT-proBNP = N-terminal fragment B-type natriuretic peptide; NYHA = New York Heart Association; PAH = pulmonary arterial hypertension; PAP = pulmonary arterial pressure; PH = pulmonary hypertension; WHO = World Health Organization.

[a]See diagnostic algorithms for suspected PH in European Society of Cardiology (ESC)/European Respiratory Society (ERS) Guidelines on Pulmonary Hypertension (2015)[208].

[b]Dasatinib-induced PH usually reversible with drug cessation.

EUROPEAN SOCIETY OF CARDIOLOGY®

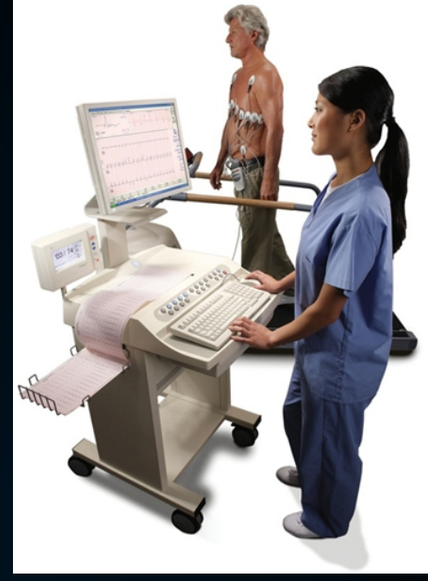
CORONARY ARTERY DISEASE

Table 7 **Pathophysiological mechanisms of coronary artery disease in cancer treatment**[7,60,81,99,117–123]

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) ponatinib	• Procoagulant status • Arterial thrombosis • Endothelial injury	• Risk of arterial thrombosis: bevacizumab 3.8%, sorafenib 1.7%, sunitinib 1.4%
Radiotherapy *… typically manifests* ***10 – 15 years after*** *the initial treatment, and* ***younger*** *patients are more susceptible*	• Endothelial injury • Plaque rupture • Thrombosis	• 2–7-fold increased relative risk of myocardial infarction • Cumulative 30-year coronary events incidence of 10% in Hogdkin lymphoma survivors • Risk proportional to irradiation dose

5-FU = 5-fluorouracil; VEGF = vascular endothelial growth factor.

DIAGNOSI di CORONAROPATIA



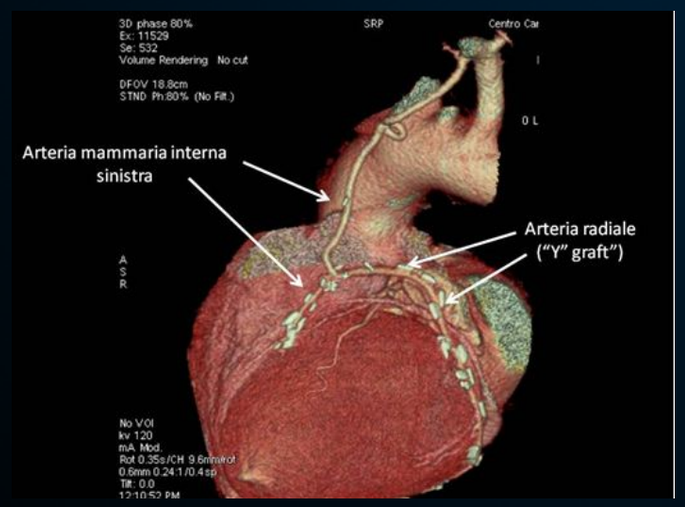
- TEST ERGOMETRICO

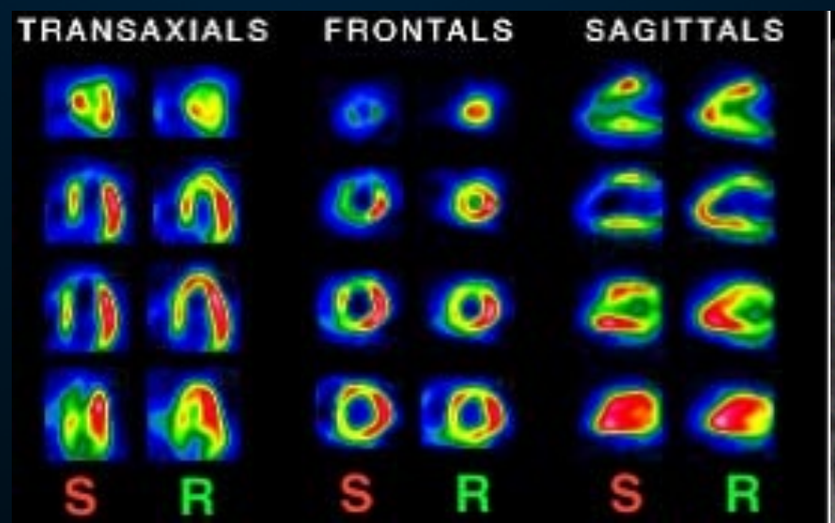
- ECOSTRESS (dpm – dobu – sforzo)
- SCINTIGRAFIA MIOCARDICA (dpm-Tc / sforzo-Tl201)

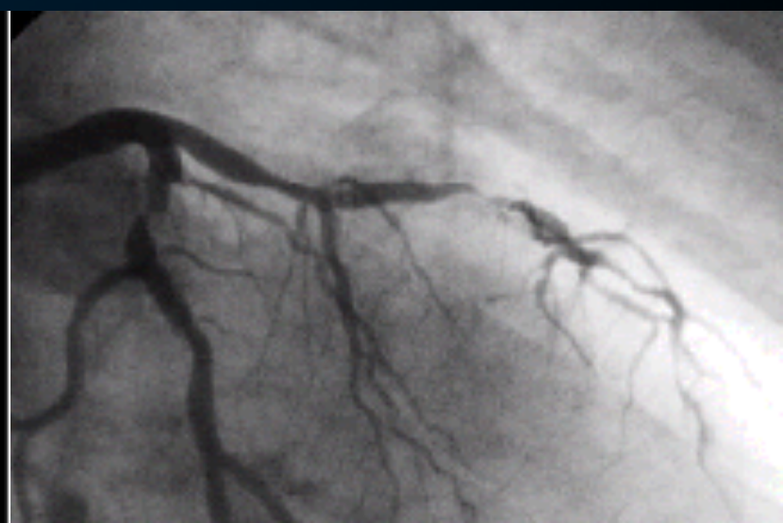
- CORONAROGRAFIA (anche coronarite da RX-terapia)

- TEST ERGONOVINA (spasmo!)

- TC CORONARICA







SCOMPENSO

CMP IPOCINETICA

CLASSIFICAZIONE AHA/ACC

STADIO A

Alto rischio per scompenso ma senza malattia cardiaca strutturale o sintomi di scompenso

STADIO B

Pazienti con malattia cardiaca strutturale ma senza sintomi di scompenso

STADIO C

Pazienti con malattia cardiaca strutturale e sintomi presenti o passati di scompenso

STADIO D

Scompenso refrattario che necessiti di interventi specializzati

Sviluppo di patologia cardiaca strutturale

Comparsa di sintomi scompenso cardiaco

Sintomi di scompenso cardiaco refrattari, a riposo

Es.
pazienti con
- ipertensione
- diabete mellito

- USO DI FARMACI CARDIOTOSSICI

- storia familiare di cardiomiopatie

Es.
pazienti con
- pregresso IMA
- disfunzione sistolica ventricolo sinistro
- valvulopatie asintomatiche

Es.
pazienti con
- malattia cardiaca strutturale nota
- dispnea, fatigabilità, ridotta tolleranza allo sforzo

Es.
pazienti con sintomi severi nonostante terapia massimale (pazienti con frequenti ospedalizzazioni che richiedono supporto terapeutico speciale)

PATIENT WITH SUSPECTED HF[a]
(non-acute onset)

ASSESSMENT OF HF PROBABILITY

1. Clinical history:
History of CAD (MI, revascularization)
History of arterial hypertension
Exposition to cardiotoxic drug/radiation
Use of diuretics
Orthopnoea / paroxysmal nocturnal dyspnoea

2. Physical examination:
Rales
Bilateral ankle oedema
Heart murmur
Jugular venous dilatation
Laterally displaced/broadened apical beat

3. ECG:
Any abnormality

All absent

≥1 present

Assessment of natriuretic peptides not routinely done in clinical practice

NATRIURETIC PEPTIDES

- NT-proBNP ≥125 pg/mL
- BNP ≥35 pg/mL

No

<u>HF unlikely:</u>
consider other diagnosis

Yes

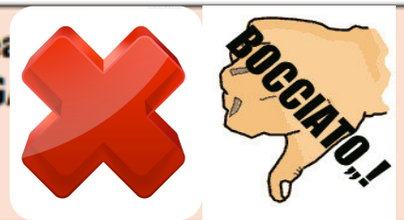
ECHOCARDIOGRAPHY

Normal[b,c]

<u>If HF confirmed (based on all available data):</u>
determine aetiology and start appropriate treatment

ESC 2016

Table 6 **Proposed diagnostic tools for the detection of cardiotoxicity**

Technique	Currently available diagnostic criteria	Advantages	Major limitations
Echocardiography: **- 3D-based LVEF** **- 2D Simpson's LVEF** **- GLS**	• LVEF: >10 percentage points decrease to a value below the LLN suggests cardiotoxicity. • GLS: >15% relative percentage reduction from baseline may suggest risk of cardiotoxicity.	• Wide availability. • Lack of radiation. • Assessment of haemodynamics and other cardiac structures.	• Inter-observer variability. • Image quality. • GLS: inter-vendor variability, technical requirements.
Nuclea **(MUG** 	• >10 percentage points decrease in LVEF with a value <50% identifies patients with cardiotoxicity.	• Reproducibility.	• Cumulative radiation exposure. • Limited structural and functional information on other cardiac structures.
Cardiac magnetic resonance	• Typically used if other techniques are non-diagnostic or to confirm the presence of LV dysfunction if LVEF is borderlines.	• Accuracy, reproducibility. • Detection of diffuse myocardial fibrosis using T1/T2 mapping and ECVF evaluation.	• Limited availability. • Patient's adaptation (claustrophobia, breath hold, long acquisition times).
Cardiac biomarkers: **- Troponin I** **- High-sensitivity Troponin I** **- BNP** **- NT-proBNP**	• A rise identifies patients receiving anthracyclines who may benefit from ACE-Is. • Routine role of BNP and NT-proBNP in surveillance of high-risk patient needs futher investigation.	• Accuracy, reproducibility. • Wide availability. • High-sensitivity.	• Insufficient evidence to establish the significance of subtle rises. • Variations with different assays. • Role for routine surveillance not clearly established.

The same imaging modality and/or biomarker assay should be used for continued screening throughout the treatment pathway

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

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Revisori del Documento
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GESTIONE del Pz oncologico a RISCHIO CV

Tempo

- **Prima della Chemioterapia**
  - Analisi dei fattori di rischio associati a:
    - Protocollo terapeutico
    - Profilo di rischio CV del paziente
  - Trattare i fattori di rischio CV modificabili
- **Durante la Chemioterapia**
  - Monitorare se alto rischio CV (paziente/terapia)
  - Eseguire la cardioprotezione
  - Trattare il danno cardiaco
- **Dopo la Chemioterapia**
  - Monitore il profilo CV e gli effetti CV tardivi
  - Intervenire per ridurre le complicanze tardive
  - Trattare il danno cardiaco

Cardiologo
+
Oncologo

+

Medico di Assistenza Primaria

FATTORI di RISCHIO CARDIOVASCOLARE

FATTORI NON MODIFICABILI

ETÀ (> 50 anni)

SESSO MASCHILE (♀menopausa)

FAMILIARITÀ

FATTORI di RISCHIO CARDIOVASCOLARE

FATTORI MODIFICABILI

DISLIPIDEMIA

FUMO

IPERTENSIONE

DIABETE

SOVRAPPESO-OBESITÀ

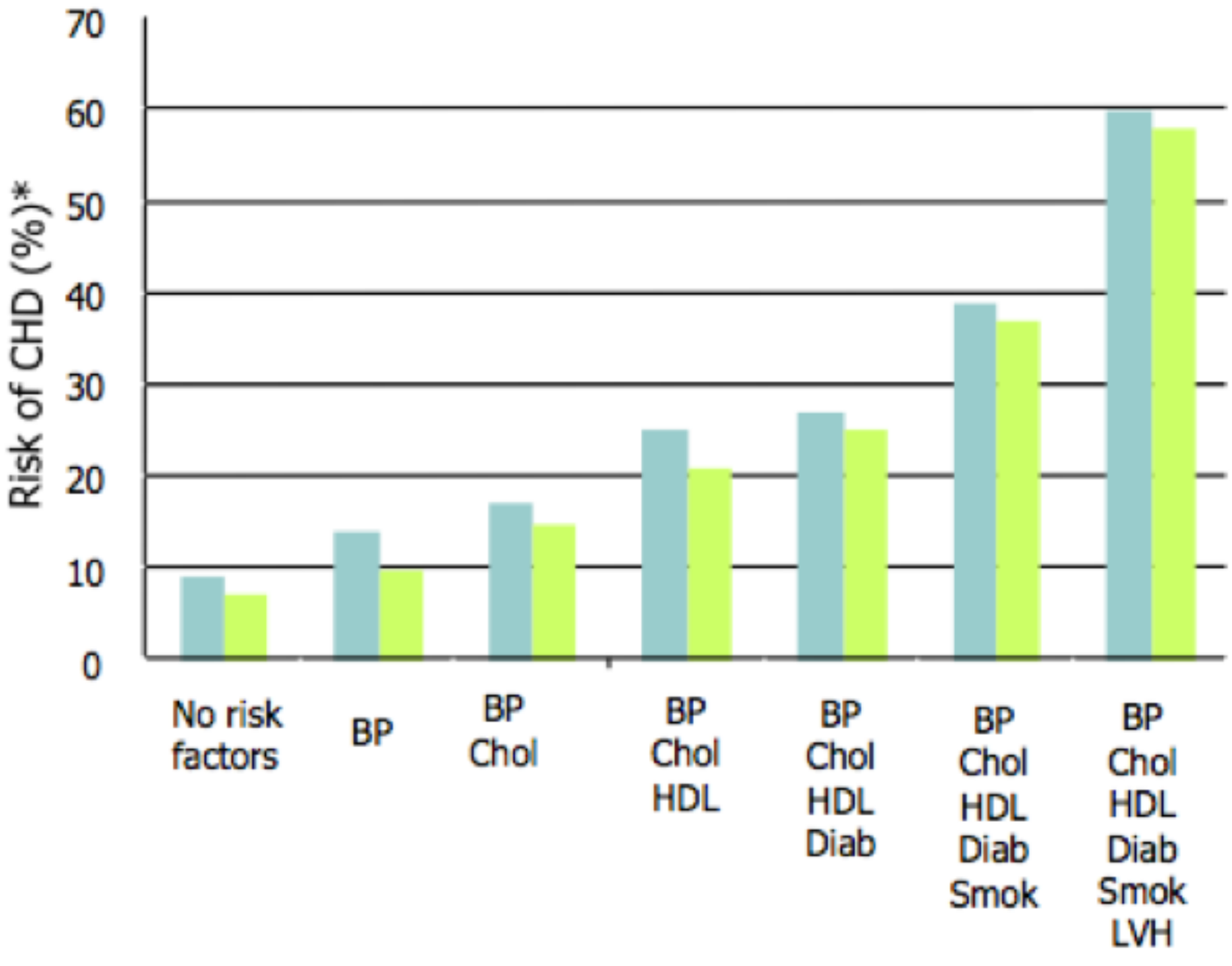
SEDENTARIETÀ

STRESS

RISK OF CORONARY HEART DISEASE INCREASES WITH MULTIPLE RISK FACTORS

EFFETTO ESPONENZIALE

Analysis of data from the Framingham Heart Study



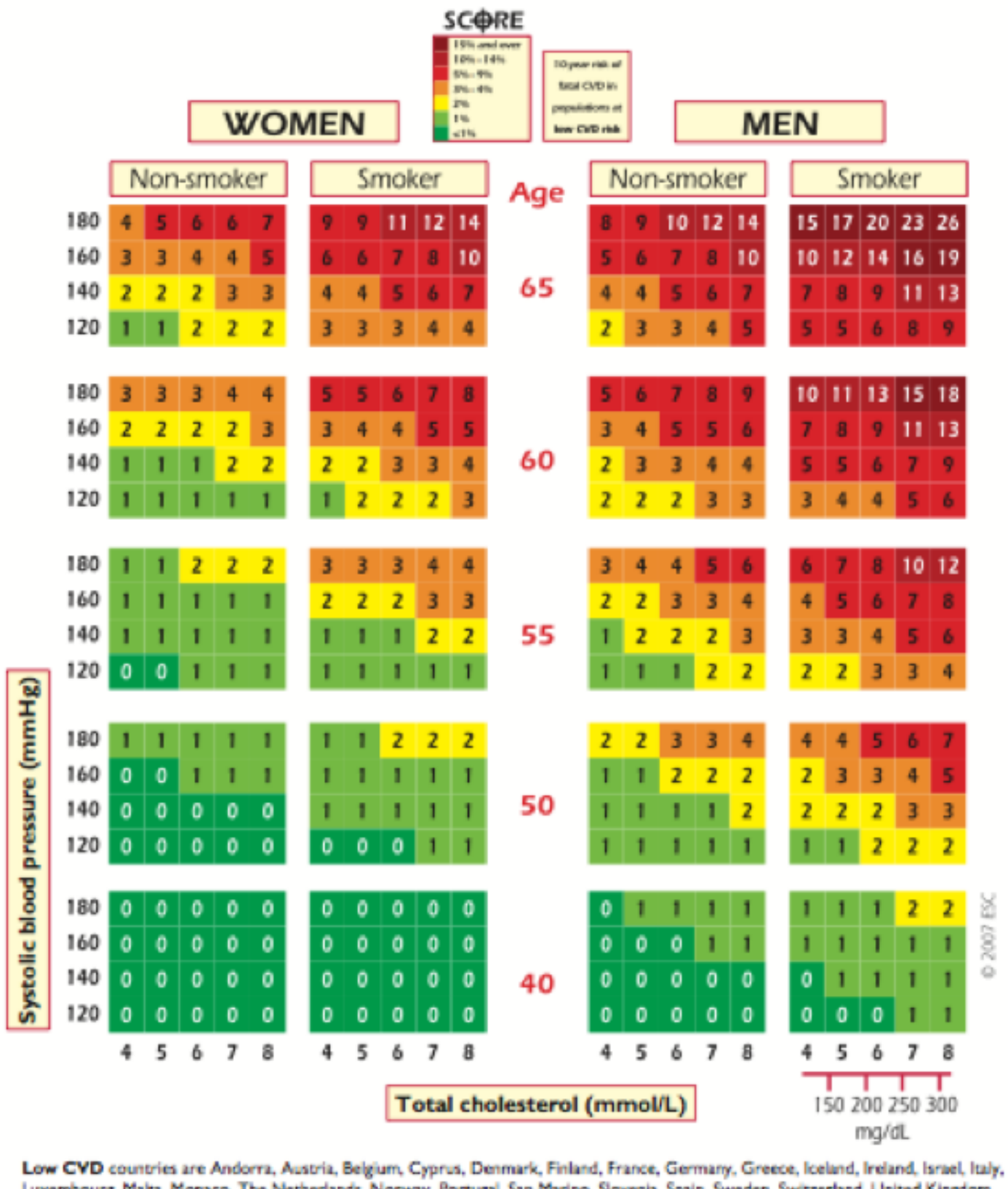
Risk factors

- Systolic Blood Pressure (>160 mm Hg)
- Cholesterol (>260 mg/dL)
- HDL cholesterol (<35 mg/dL)
- Diabetes
- Smoking
- Left ventricular hypertrophy confirmed by ECG

Men

Women

Kannel, Hypertens Res 1995



Low CVD countries are Andorra, Austria, Belgium, Cyprus, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Luxembourg, Malta, Monaco, The Netherlands, Norway, Portugal, San Marino, Slovenia, Spain, Sweden, Switzerland, United Kingdom.

Figure 4 SCORE chart: 10-year risk of fatal cardiovascular disease (CVD) in countries at low CVD risk based on the following risk factors: age, sex, smoking, systolic blood pressure, and total cholesterol. Note that the risk of total (fatal + non-fatal) CVD events will be approximately three times higher than the figures given.

HeartScore

Stratificazione Pts in **4 gruppi** di rischio:

- **basso**
- **moderato**
- **alto**
- **molto alto**

*Il numero riportato nelle celle rappresenta il rischio di **eventi CV fatali a 10 anni** espresso in valore assoluto **%***

Paesi a Basso Rischio

RISK AGE

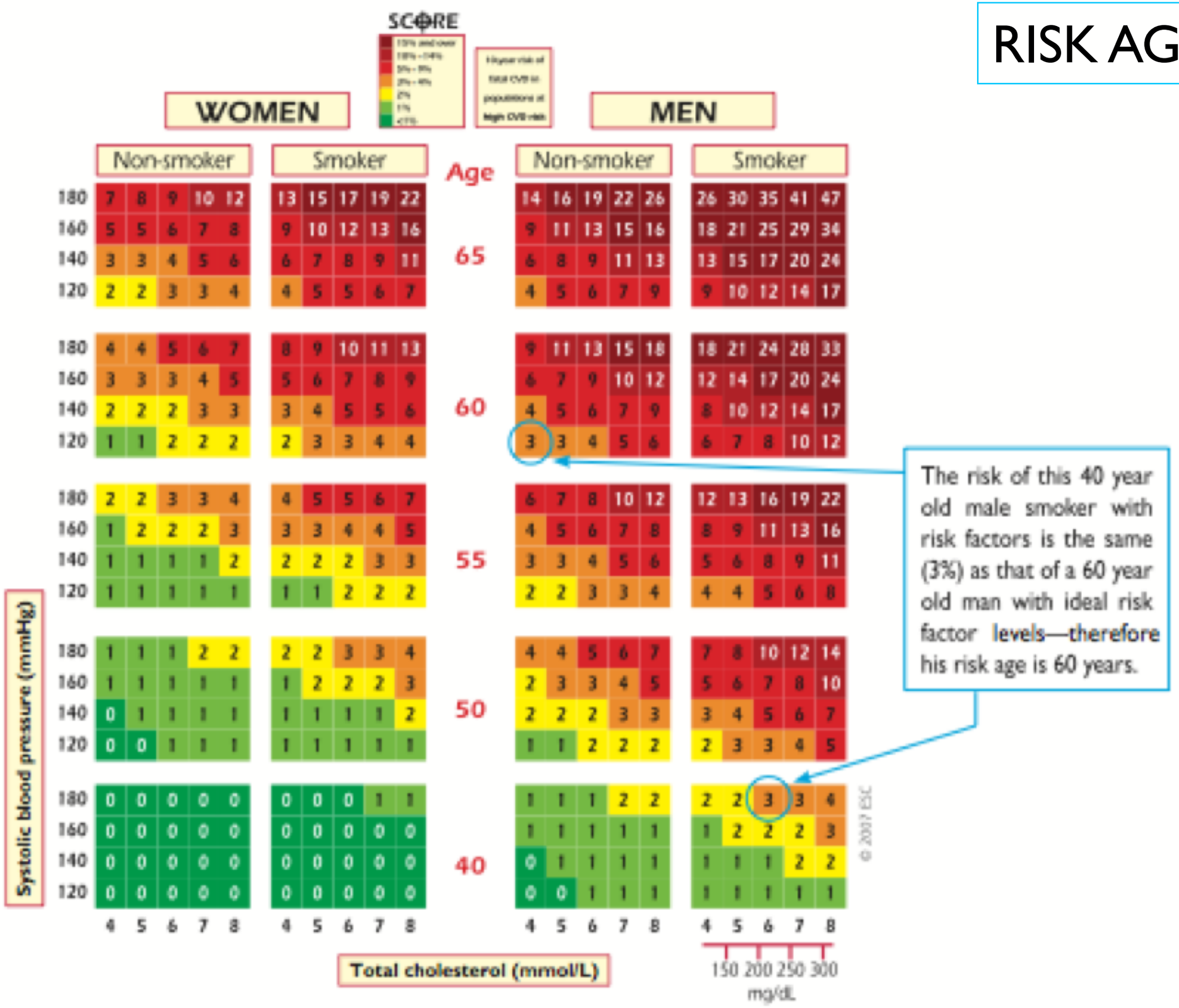


Figure 6 Illustration of the risk–age concept.

LIMITI degli ALGORITMI

- Le carte si fermano a 69 anni
- Non considerati:
  - **Pressione diastolica**
  - **C-LDL**
  - **Sovrappeso / obesità**
  - **Sedentarietà**
  - **Famigliarità**
  - **Malattia renale (GFR < 60 ml/min/1.73m^2)**
  - **Placche carotidee**
  - **Stato sociale**
  - **Informazioni di tipo probabilistico** (possibili eventi CV durante CT anche in Pts a rischio basso o in assenza di noti FRC)

CATEGORIA DI RISCHIO	PUNTEGGIO (SCORE)	CARATTERISTICHE DEI SOGGETTI
Molto alta	≥10%	Soggetti con: • malattia CV documentata mediante test invasivi e non invasivi; • precedente infarto del miocardio; • sindrome coronarica acuta; • rivascolarizzazione coronarica; • stroke ischemico; • arteriopatia periferica; • diabete di tipo II, diabete di tipo I con markers di danno d'organo; • patologia renale cronica moderata-severa (FG <60 ml/min/1.73m^2).
Alta	≥5% e <10%	Soggetti con: • SCORE ≥5% e <10% • singoli fattori di rischio marcatamente elevati come dislipidemie familiari e ipertensione severa.
Moderata	≥1% e <5%	Soggetti con: • SCORE ≥1% e <5% Il rischio è ulteriormente influenzato da: • storia familiare di patologia coronarica precoce; • obesità addominale; • attività fisica; • Col-HDL, TG, CRP ad alta sensibilità, Lp(a), fibrinogeno, omocisteina, Apo B; • classe sociale.
Bassa	<1%	

DISLIPIDEMIA

OBESITÀ

DIABETE

PROCESSO ATEROGENETICO

FUMO

SEDENTARIETÀ

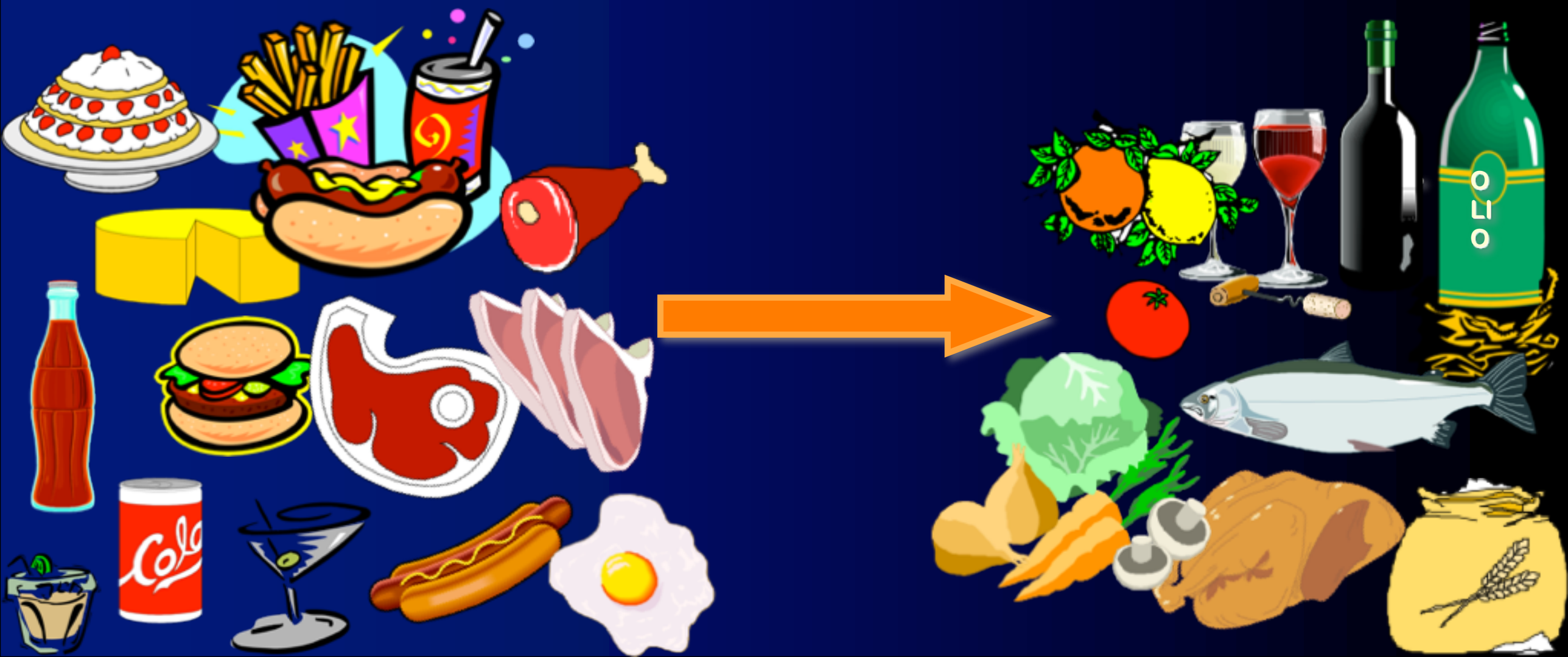
IPERTENSIONE

STRESS

ALIMENTAZIONE CORRETTA

RIDUZIONE DELL'APPORTO DI ZUCCHERI SEMPLICI, GRASSI SATURI E COLESTEROLO

DIETA MEDITERRANEA !



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October
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2018
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GIORNATE CARDIOLOGICHE TORINESI