Cardiac emergencies in patients with cancer

KRISTINE JANG, D.O., FACC

STONY BROOK UNIVERSITY HOSPITAL

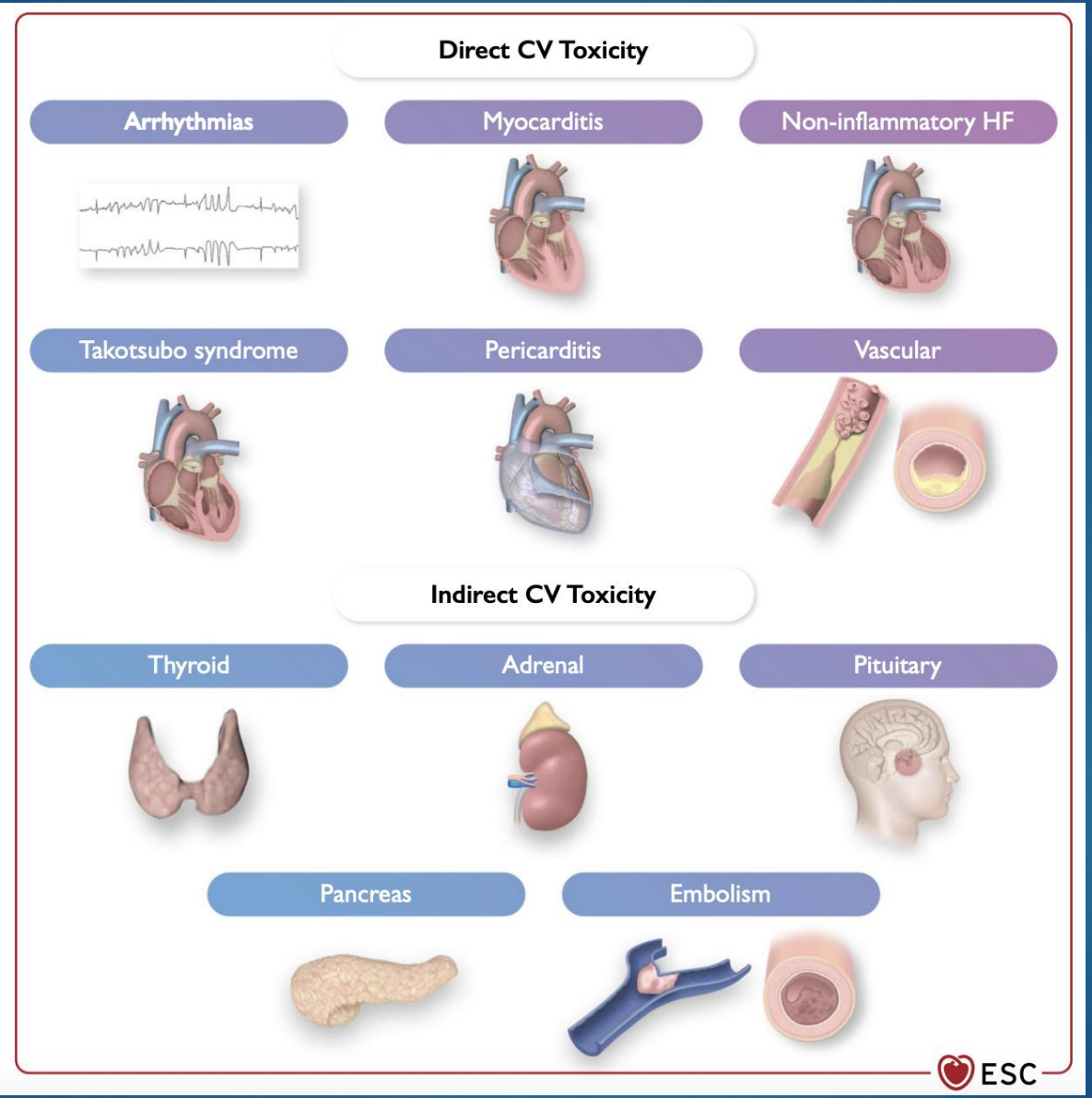
Learning objectives

Identify and manage cardiovascular emergencies that are related to **cancer itself**

Understand cardiovascular emergencies that are associated with **cancer therapy**

Cardiovascular emergencies in patients with cancer

- **Arrhythmia**
- **Acute Coronary Syndrome**
- **Heart failure and myocarditis**
- Hypertensive emergencies
- Pericardial disease



Alexander R Lyon, et al. *European Heart Journal*, Volume 43, Issue 41, 1 November 2022, Pages 4229–4361, https://doi.org/10.1093/eurheartj/ehac244

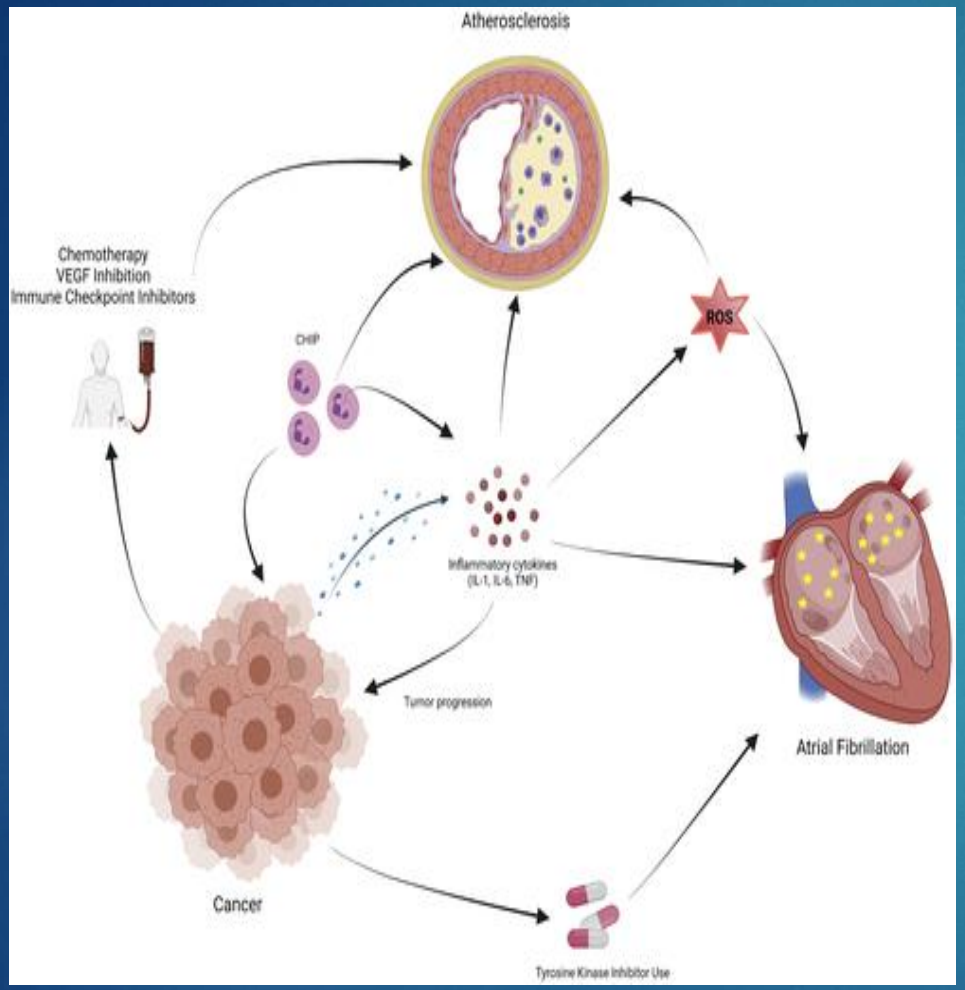
Arrhythmia in cancer patients

- Due to cancer itself
  - metastatic/infiltrative process, carcinoid
- Due to therapy
  - surgery, radiation, chemotherapeutic agents
- In cancer patients, we should not only think about the rhythm itself but the possible underlying causes.
- Examples
  - **Atrial arrhythmia** in pulmonary embolism and pulmonary issues secondary to cancer itself or cancer therapy related
  - **Wide complex tachycardia** due to ACS, secondary to electrolyte imbalance or metabolic derangement secondary to cancer itself or cancer therapies

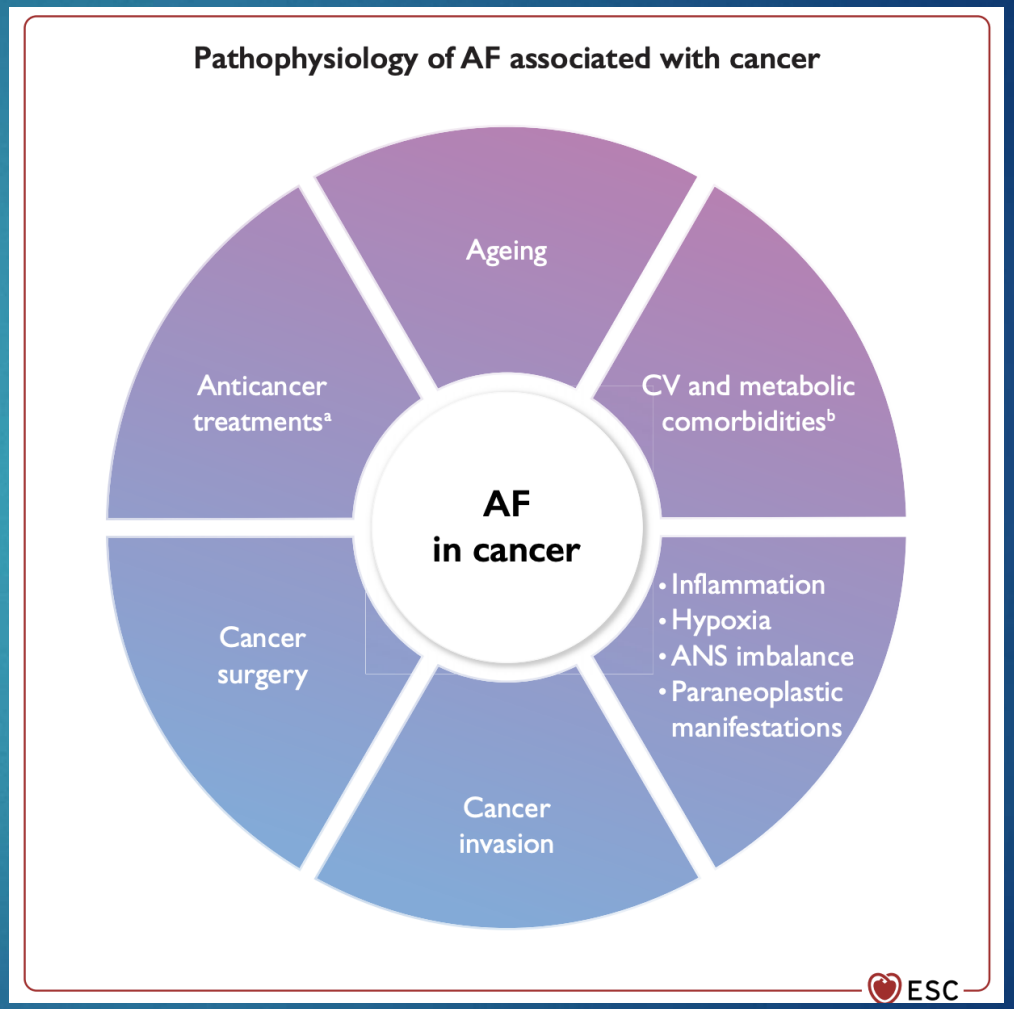
Arrhythmia in cancer patients

- **Tachyarrhythmia**
  - Atrial arrhythmia- afib, aflutter
  - Ventricular tachyarrhythmia
  - QT prolongation leading torsade de pointe
- **Bradyarrhythmia**
  - AV conduction disease especially in patients on immune checkpoint therapy in the presence of myocarditis
  - Sinus bradycardia associated with Immunomodulatory drugs (thalidomide, pomalidomide) and ALK inhibitors (crizotinib, alectinib, brigatinib, or ceritinib). Usually, patient can tolerate it well without symptoms.

Atrial fibrillation in patients with cancer



Orly Leiva et al. *J Am Coll Cardiol CardioOnc* 2021; 3:619-634.



Alexander R Lyon, et al. *European Heart Journal*, Volume 43, Issue 41, 1 November 2022, Pages 4229–4361, https://doi.org/10.1093/eurheartj/ehac244

Diagnosis and management

- **Assessment of hemodynamic stability in addition to assessing heart failure and shock** is important part of the assessment and management. Consider DCCV for an appropriate candidate.
- Consider **drug drug interactions and QT prolongation** when using a therapy (patient may already be on QT prolonging therapy
- Choice of **anticoagulation** for stroke prevention and potential concerns for disrupting therapy when patient has thrombocytopenia from cancer therapy or cancer related surgeries and procedures

QTc prolonging cancer therapy agents

Classification	Drugs
High risk: QTcF prolongation ≥ 10 ms and risk of TdP	• Aclarubicin • Arsenic trioxide • Glasdegib • Nilotinib • Oxaliplatin • Pazopanib • Ribociclib • Sunitinib • Toremifene • Vandetanib
Moderate risk: QTcF prolongation ≥ 10 ms and low or no risk of TdP (or uncertain)	• Abarelix • Belinostat • Brigantinib • Carbozantinib • Ceritinib • Crizotinib • Dovitinib • Entrectinib • Eribulin • Gilteritinib • Ivosidenib • Lapatinib • Lenvatinib • Osimertinib • Panobinostat • Rucaparib • Selpercatinib • Sorafenib • Tipiracil/ trifluridine • Vemurafenib

Chaftari, P., Mouhayar, E., Iliescu, C., Hassan, S.A., Kim, P. (2016). Cardiac Emergencies in Cancer Patients. In: Manzullo, E., Gonzalez, C., Escalante, C., Yeung, SC. (eds) Oncologic Emergencies. MD Anderson Cancer Care Series. Springer, New York, NY. https://doi.org/10.1007/978-1-4939-3188-0_3

Classes of QT prolonging medications

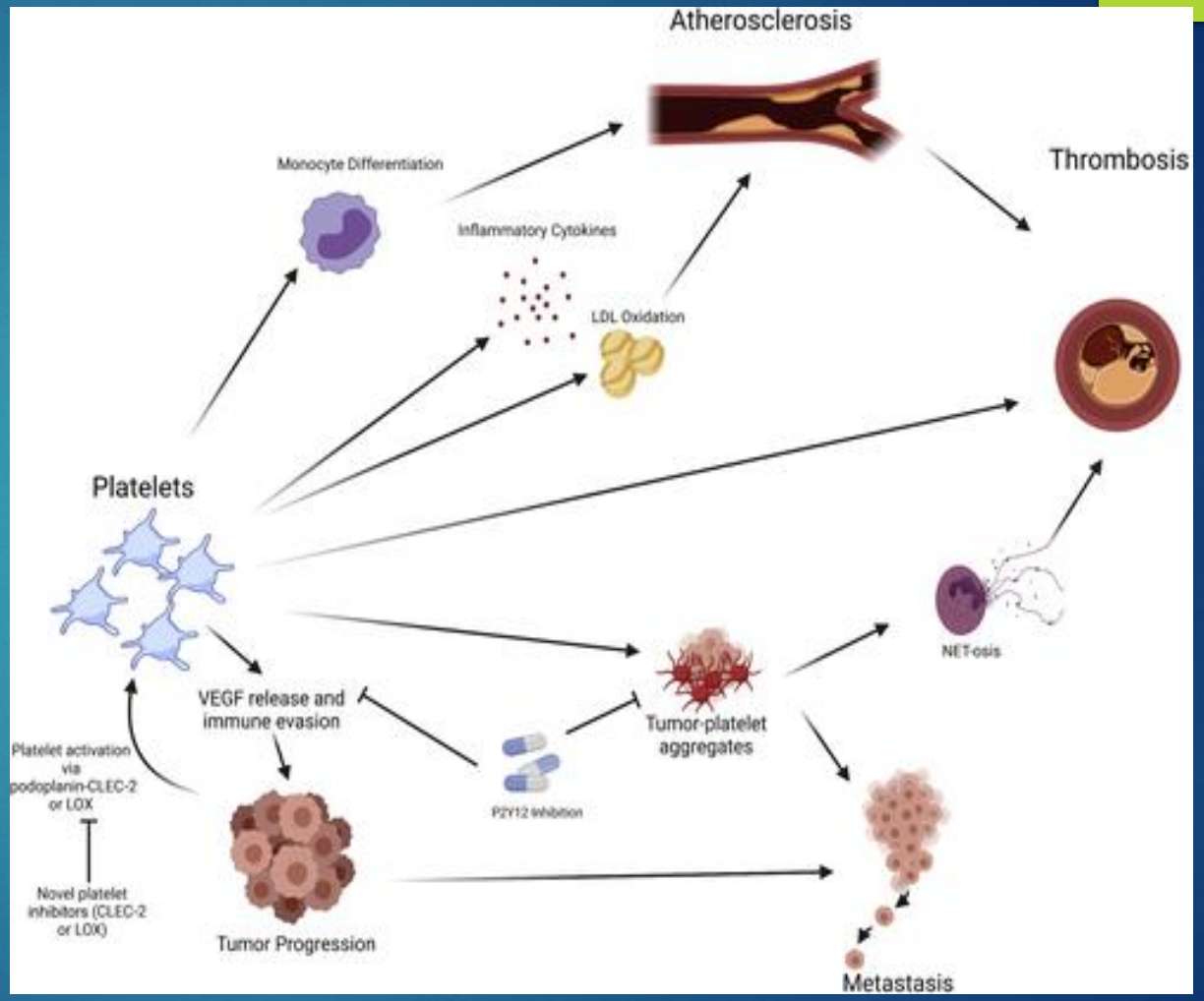
Correctable	Non-correctable
QT-prolonging drugs[a] • Antiarrhythmics • Antibiotics • Antidepressants • Antifungals • Antiemetics • Antihistamines • Antipsychotics • Loop diuretics • Opioids (methadone) Bradyarrhythmia Electrolyte imbalance/ abnormalities • Hypokalaemia (≤3.5 mEq/L) • Hypomagnesaemia (≤1.6 mEq/L) • Hypocalcaemia (≤8.5 mEq/L) Inadequate dose adjustment of renal or hepatic cleared QT-prolonging drugs	Acute myocardial ischaemia Age > 65 years Baseline QTc interval prolongation[b] Family history of sudden death (congenital LQTS or genetic polymorphism) Female sex Impaired renal function (for renally excreted drugs) Liver disease (for hepatically excreted drugs) Personal history of syncope or drug-induced TdP Pre-existing CVD (CAD, HF, LV hypertrophy)

Chaftari, P., Mouhayar, E., Iliescu, C., Hassan, S.A., Kim, P. (2016). Cardiac Emergencies in Cancer Patients. In: Manzullo, E., Gonzalez, C., Escalante, C., Yeung, SC. (eds) Oncologic Emergencies. MD Anderson Cancer Care Series. Springer, New York, NY. https://doi.org/10.1007/978-1-4939-3188-0_3

Acute coronary syndrome in cancer patients

- Data in this area is limited to observational and registry data

Coronary artery disease in cancer patients



Orly Leiva et al. *J Am Coll Cardiol CardioOnc* 2021; 3:619-634.

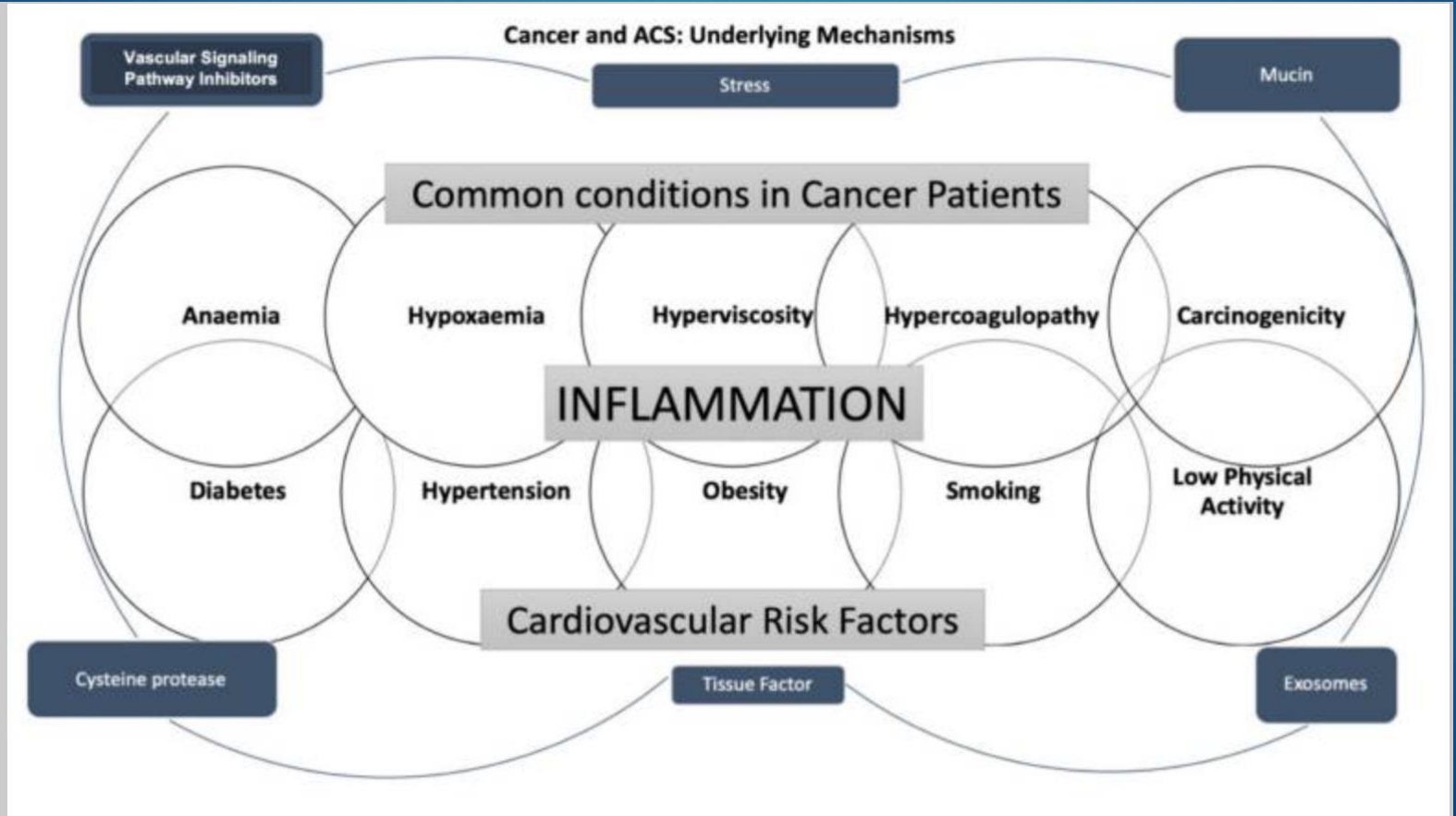
Definition

- UA
- NSTEMI
- STEMI

- Plaque rupture or coronary thrombosis
- O2 supply and demand mismatch
- MI with Nonobstructive coronary arteries
- Takotsubo syndrome

- Additional factors to consider in cancer patients:
- Cancer therapy -
  - Antimetabolites such as 5FU induced coronary vasospasm
  - VEGF inhibitor like bevacizumab

Mechanisms of the associations between cancer and acute coronary syndrome



Lucà F, Parrini I, Abrignani MG, Rao CM, Piccioni L, Di Fusco SA, Ceravolo R, Bisceglia I, Riccio C, Gelsomino S, Colivicchi F, Gulizia MM. Management of Acute Coronary Syndrome in Cancer Patients: It's High Time We Dealt with It. J Clin Med. 2022 Mar 24;11(7):1792. doi: 10.3390/jcm11071792. PMID: 35407399; PMCID: PMC8999526.

Diagnosis

- History *
  - New HF or ventricular arrhythmia- have the suspicion, new murmur, hemodynamic instability, cardiac arrest
- Assessment of risk factors
  - Traditional risk factors to consider: male, DM, HTN, HLD, smoking hx, CVA/TAI, PAD etc
  - Cancer therapy related risk factors: Irradiation to the chest/mediastinum
- Serial EKG's and cardiac enzymes (troponin I or T, more specific and reliable over creatinine kinase and its isoenzymes
  - ST elevation (STEMI)
  - ST depressions, T wave flattening, T wave inversions etc (However, this is not only limited to ACS)
    - Patients with metastatic disease (involving myocardium), pulmonary embolism, brain lesions etc
- Echocardiogram

Management of ACS in patients with cancer

- Challenges of managing ACS in cancer patients
  - Frailty
  - Increased bleeding risk, thrombocytopenia
  - Increased thrombotic risk
  - Possible need future procedures and surgery
- We not only have to manage promptly but we also have to prevent patients from receiving potential therapy that may cause further harm
  - Anticoagulation or dual antiplatelet therapy in patients with thrombocytopenia
  - Conservative management of ACS in patients with poor prognosis

Medical and invasive therapy for ACS

- Medication therapy – anti-ischemic therapy
  - BB, ACEi, …etc
  - Antiplatelet therapy, anti thrombotic therapy
  - Anti inflammatory and lipid lowering
- Early invasive therapy vs conservative
- Multidisciplinary discussion
  - Discuss with the oncologist, ER, critical care, and cardiologist.
- Understanding patient's prognosis, current and past treatment is a key.

Decompensated heart failure in cancer patients

- Understanding their risk factors and history is important
  - Baseline cardiac risk factors and cardiac history
  - Type of cancer and chemotherapeutic agents that the patient is exposed to
    - Additionally, understanding the cumulative dose, concomitant therapy and administration schedule are important
      - Anthracycline –cumulative dose
      - Timing of immunotherapy administration – incidence is higher in the first 1-2 months(?)
- Presentation
  - Acute decompensated heart failure
  - Cardiogenic shock
  - Right heart failure
  - Myocarditis
  - Stress cardiomyopathy or Takotsubo cardiomyopathy

Heart Failure emergencies- chemotherapeutic

- Anthracyclines
  - Doxorubicin, epirubicin, idarubicin, daunorubicin etc
- Monocloncal antibody-based tyrosine kinase inhibitors
  - Trastuzumab
  - Bevacizumab
- Small-molecule tyrosine kinase inhibitors
  - Dasatinib
  - Imatinib
  - Sunitinib
- Alkylating agents
  - Cyclophosphamide
  - Ifosfamide
- Immune check point inhibitors
- *Antimetabolities*
  - *clofarabine*

Cardiac causes

- Acute MI
- Mechanical complications of MI
- Valvular disease, AS, AI, MS, MR
- Infiltrative disease including amyloidosis
- Takotsubo or stress cardiomyopathy
- Peripartum cardiomyopathy
- Myocarditis (viral or immune checkpoint inhibitor)
- Toxic or metabolic (alcohol induced, thyroid illness et)
- Chemo

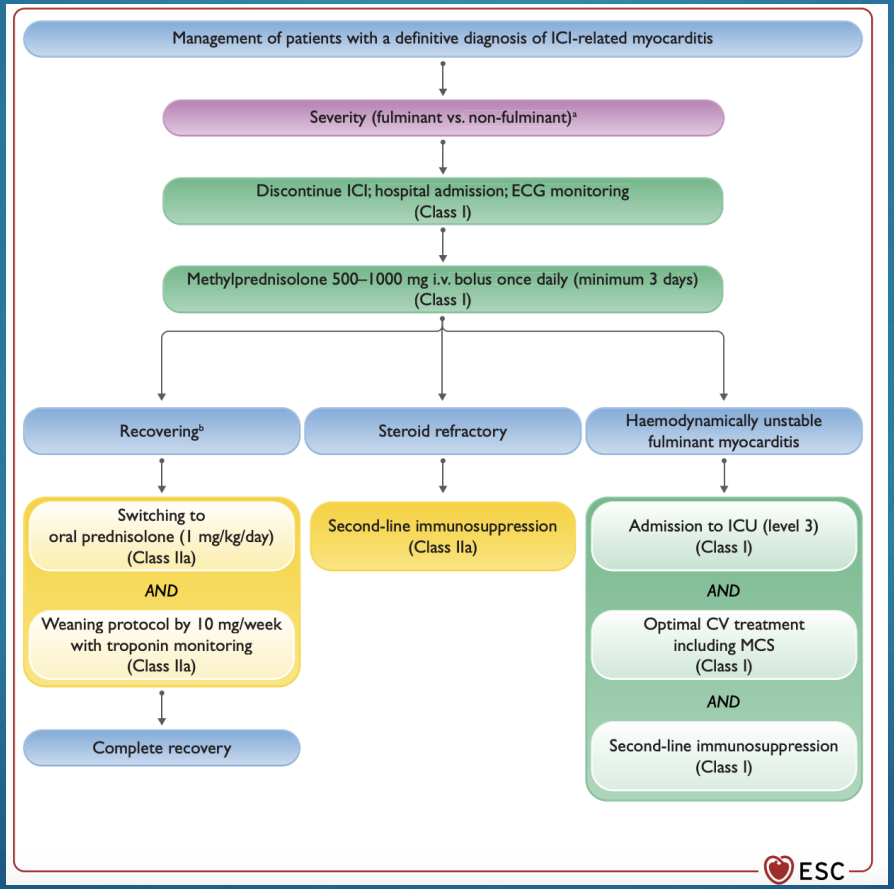
Diagnostic test

- Basic labs- CBC, chem, trop, BNP/nt proBNP, liver function, lactate etc
- EKG
- CXR
- Echocardiogram
- Cardiac catheterization

Treatment

- Diuretic therapy
- Oxygenation including NPPV
- Vasodilator therapy in the case of hypertensive acute HF
- Inotropic or pressor support
- Mechanical devices including IAPB, temporary LV assist devices like Impella –to partial unloading of LV to reduce myocardial demand, increase cardiac output leading to increase end organ perfusion

Immune check point inhibitor induced Myocarditis



Alexander R Lyon, et al. *European Heart Journal*, Volume 43, Issue 41, 1 November 2022, Pages 4229–4361, https://doi.org/10.1093/eurheartj/ehac244

Hypertensive urgency and emergency

- HTN is one of the most common cardiac risk factors in cancer patients.
- HTN is also one of the most adverse effects due to the cancer therapeutics.
  - Most notably vascular signaling pathway inhibitors
    - Anti vascular endothelial growth factor antibody bevacizumab
    - Tyrosine kinase inhibitors (sunitinib, sorafenib, pazopanib)
      - mechanism-
- Another mechanism is by progression of atherosclerotic process of renal artery stenosis over time

Management of hypertensive crisis

Drug	Dose	Indications/mechanism of action	Adverse effects
Sodium nitroprusside	0.25–10 mcg/kg/min	Any patient; venous and arterial vasodilator	Cyanide toxicity, nausea, vomiting
Labetalol	20–80 mg IV bolus followed by drip at 0.5–2.0 mg/min or 20–80 mg IV every 15 min	Any patient except those with decompensated heart failure	Orthostatic hypotension, heart failure exacerbation, bradycardia
Nicardipine	5–15 mg/h	Any patient, caution in patients with angina; calcium channel blocker vasodilator	Reflex tachycardia, nausea, vomiting
Nitroglycerin	5–200 mcg/min	Acute myocardial infarction, angina, or heart failure symptoms; vasodilator	Headache, nausea, tachyphylaxis
Hydralazine	5–10 mg IV every 4–6 h (not to exceed 20 mg/dose)	Any patient, avoid in patients with acute myocardial infarction; vasodilator	Reflex tachycardia, headache, angina exacerbation
Enalaprilat	0.625–1.250 mg IV every 6 h	Avoid in patients with acute myocardial infarction, renal failure, or hyperkalemia; ACE inhibitor	Renal insufficiency, hyperkalemia
Fenoldopam	0.1–1.6 mcg/kg/min	Any patient; calcium channel blocker vasodilator	Hypotension, headache, angina exacerbation
Esmolol	500-mcg/kg bolus over 1 min followed by 50–300 mcg/kg/min by infusion	Avoid in patients with underlying bradycardia or decompensated congestive heart failure; β-blocker	First-degree heart block, congestive heart failure, asthma
Phentolamine	5–10 mg as IV bolus, 1–2 min/10–30 min	Pheochromocytoma; hypertensive crisis	Tachycardia, orthostatic hypotension, angina exacerbation

Pericardial disease

- Pericarditis, pericardial effusion, and tamponade
- Constrictive pericarditis
- Causes
  - Malignancy- direct involvement of the myocardium and pericardium
  - Infection
  - Cancer therapy
  - Chest irradiation
  - Chest/mediastinal surgery
- **What matters?** Size of the effusion, the rate of its growth
  - Tamponade -Hemodynamic status would determine urgent pericardiocentesis vs monitoring

Key points

- Management of cardiac emergencies in cancer patients is challenging and requires multi disciplinary effort
- Good history taking that involves recognition of cancer type, treatment, underlying cardiac risk factors and cardiac disease is important in providing appropriate care to cancer patients

Thank you