

# ACC Case Challenges

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# Case 1 - Atrial Fibrillation and Anticoagulation in the Cancer Patient with Thrombocytopenia

- **66 y/o female** with mild **HTN** and a remote h/o of self terminating **post-operative AF** (< 24 hrs) s/p cholecystectomy
- Exercises regularly at least 30 minutes per day of aerobic activity
- Recently diagnosed with a large gastric leiomyosarcoma. Started on **Adriamycin at 75 mg/m<sup>2</sup> with Ifosfamide 10 gm/m<sup>2</sup>**
- After her 2<sup>nd</sup> cycle she develops a **neutropenic fever** with Hgb 7.8, **Platelets 38**, and wbc 0.9 at nadir and an ECG consistent with atrial fibrillation with RVR. Hemodynamics stable.

*How would you manage this patient's atrial fibrillation? How does this change if it is paroxysmal or persistent?*

*What are the components of your diagnostic workup?*



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# Diagnostic Workup

- CHA<sub>2</sub>DS-VASC<sub>2</sub> score = 3
- Echocardiogram with an EF 60-65%, LA size: 50 mm, GLS -21% (no valvular disease)
- Nuclear Treadmill Stress Test shows normal myocardial perfusion with a calcium score of 347, primarily in the LAD territory and an EF of 75%
- Lipid panel reveals: TC 193, HDL 58, TG 65, LDL 121



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## Case 1 Continued...the story is never over

- Neutropenic fever treated with supportive care and antibiotics with resolution after 3 days
- AF is rate controlled with beta blockade which self terminates once acute febrile episode resolves
- Upon discharge, she continues to complain of palpitations.
- Event recorder shows paroxysmal atrial fibrillation of short duration occurring during her next neutropenic episode. She continues to become pancytopenic during these episodes with platelets decreasing as low as 10.

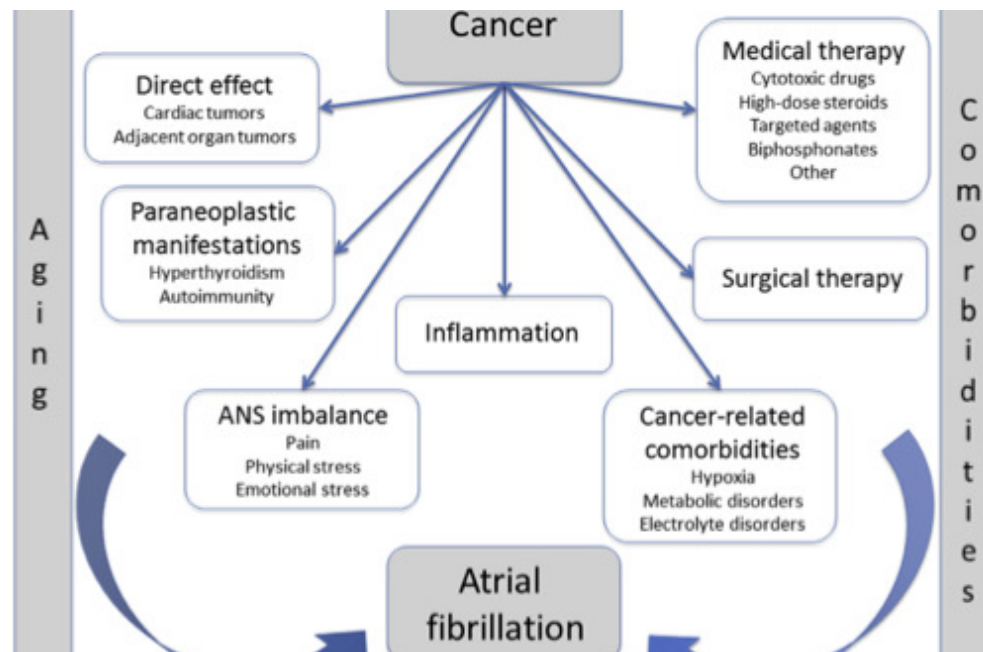
*How would you manage her atrial fibrillation and anticoagulation?*

*Would you stop her chemotherapy?*



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# Atrial Fibrillation in Cancer



Farmakis et al. JACC Vol 63, No 10, 2014: 945-53



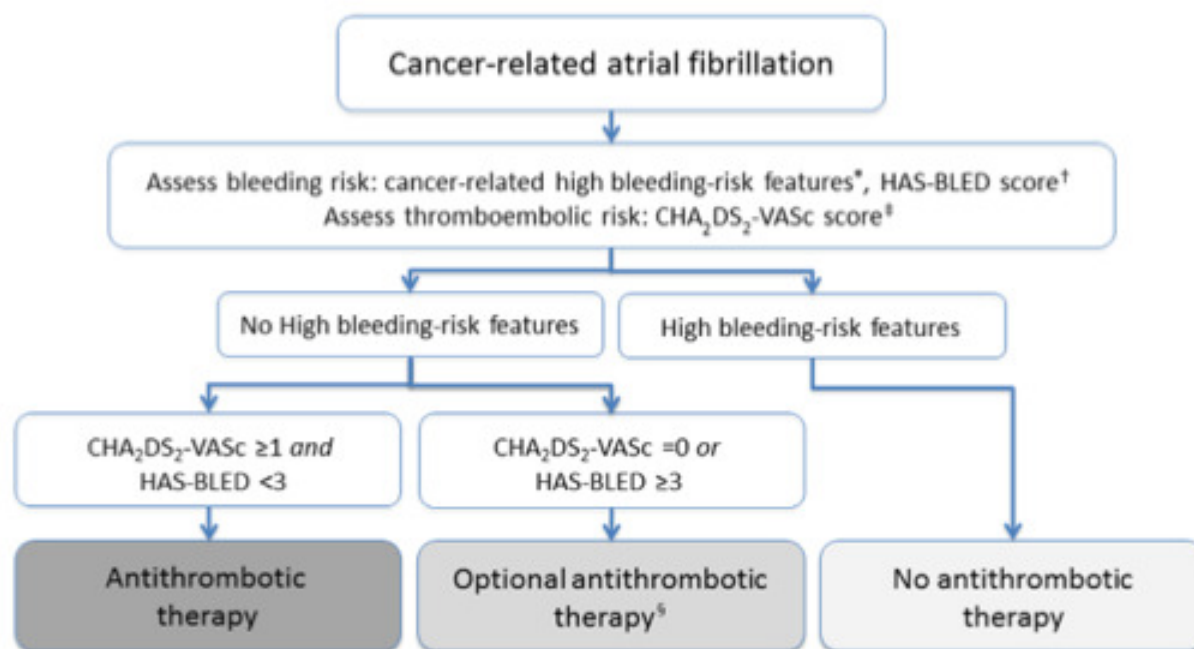
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# Chemotherapy Agents Associated with Atrial Fibrillation

- Cisplatin
- 5-fluorouracil
- Doxorubicin
- Paclitaxel/Docetaxel
- Ifosfamide
- Gemcitabine
- Mitoxantrone
- Some TKIs – Ibrutinib
- Melphalan



# Suggested Algorithm for Antithrombotic Therapy In Cancer Related Atrial Fibrillation



Farmakis et al. JACC Vol 63, No 10, 2014: 945-53

## Useful References

- Farmakis, et al. Atrial Fibrillation In Cancer. JACC 2014; 63 (10): 945-53
- Zamorano, et al. 2016 ESC Position Paper On Cancer Treatments And Cardiovascular Toxicity. European Heart Journal 2016; 37 (36): 2768-2801
- Short, et al. New Oral Anticoagulants And The Cancer Patient. The Oncologist 2014; 19 (1): 82-93
- Lee, et al. Tinzaparin vs Warfarin For Treatment Of Acute Venous Thromboembolism In Patients With Active Cancer. JAMA 2015; 314 (7): 677-686
- Lee, et al. Low Molecular Weight Heparin Versus A Coumarin For The Prevention Of Recurrent Venous Thromboembolism In Patients with Cancer. NEJM 2003; 349: 146-53



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## Case 2

**59 y/o male with Waldenstrom's macroglobulinemia (2013), well controlled HTN** treated with Coreg and Zestril.

Waldenstrom's was initially treated with rituximib, but discontinued secondary to a severe allergic response. He proceeded to bortezomib and dexamethasone with mild progression of lymphadenopathy, and was placed on **ibrutinib**.

After **6 weeks** of ibrutinib, he first noted **palpitations and lightheadedness**. He then developed **syncope and was found to have recurrent VT** with Torsades and VF requiring multiple episodes of defibrillation (29 shocks). VT is refractory to multiple medications requiring ECMO support for 3 days. **His LVEF is mildly depressed at 35%.**



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07-OCT-1957 (57 yr)  
Male      Caucasian

Vent. rate	76	BPM
PR interval	118	ms
QRS duration	94	ms
QT/QTc	446/501	ms
P-R-T axes	+ 47	17

NORMAL SINUS RHYTHM  
ANTEROLATERAL ST & T WAVE ABNORMALITY, CONSIDER ISCHEMIA  
PROLONGED QT INTERVAL, OR T U FUSION. CONSIDER MYOCARDIAL DISEASE, ELECTROLYTE  
IMBALANCE, OR DRUG EFFECTS  
WHEN COMPARED WITH ECG OF 11-AUG-2015 21:36  
CRITERIA FOR SEPTAL INFARCT ARE NO LONGER PRESENT  
T WAVE INVERSION NOW EVIDENT IN INFERIOR LEADS  
T WAVE INVERSION LESS EVIDENT IN LATERAL LEADS  
ST MORE DEPRESSED IN ANTERIOR LEADS  
\*\*\*

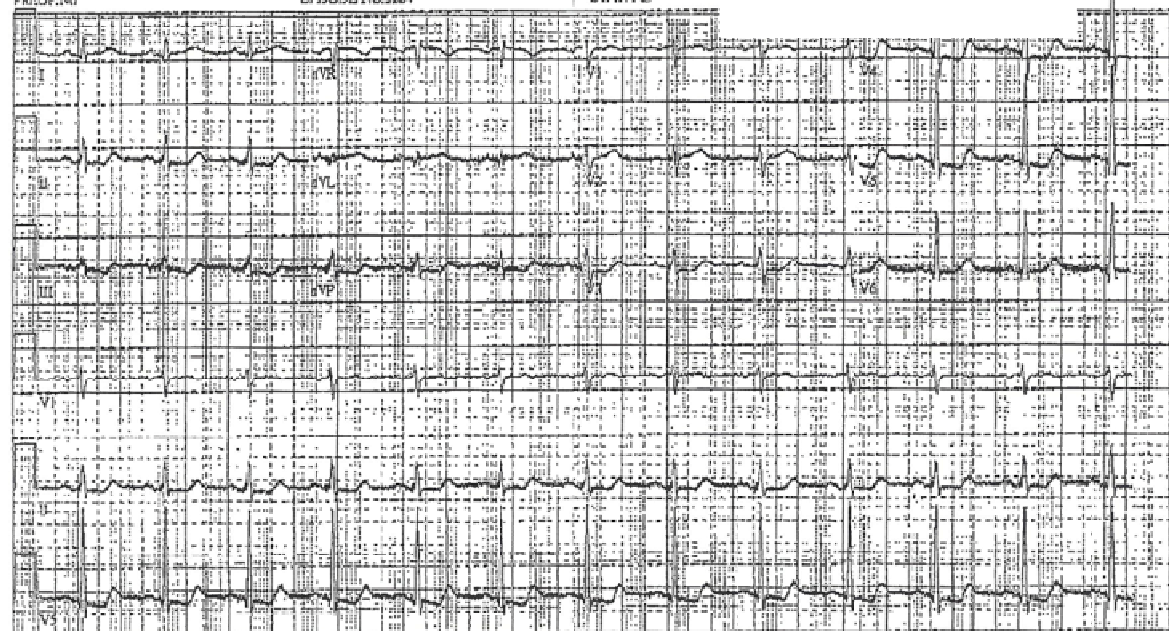
Technician: NLS  
Test Ind: Arrhythmia-

Referred by: James Wilks  
STAT: Yes

Confirmed By: RAJIB V. GORAYA, M.D.

PHOB: No

EPISODE NO: 5224



25mm/s 10mm/mV 150Hz 8.0 SP2 12SL 339 C10: 13

SID: 00040473 EID: 1014 EDT: 11:07 12-AUG-2015 ORDER: 3N790491 ACCOUNT: 012583165224

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## Case 2

He is transferred on several agents including IV amiodarone and lidocaine drips. On arrival, his QT is prolonged approaching 600 milliseconds after correction for underlying rate. He has no family history of unexplained syncope or sudden cardiac death.

*Would you have done anything differently prior to starting Ibrutinib?*

*What diagnostic tests should you obtain?*



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## Case 2

- Cardiac Catheterization: No coronary artery disease.
- Echo after ECMO removal: EF 70-75%, otherwise unremarkable.

*What is long term management of this patient?*

*How should you monitor this patient?*



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# Chemo Agents Prolonging QT

- TKIs (nilotinib, sunitinib, vandetinib)
- HDAC Inhibitors (Histone Deacetylase)
- Vascular Disruption Agents
- Arsenic Trioxide



## Useful References

- <http://oncologypro.esmo.org/Guidelines-Practice/Drug-Drug-Interactions-with-Kinase-Inhibitors/Types-of-Drug-Drug-Interactions/QT-Prolongation>
- Fradley, Michael, et al. The QT Interval Conundrum in Cancer Patients – ACC.org Cardio-oncology Website (<http://www.acc.org/cardio-oncology>)
- Fradley, Michael, et al. Electrophysiologic Considerations in Cardio-Oncology. ACC.org Cardio-oncology Website (<http://www.acc.org/cardio-oncology>)



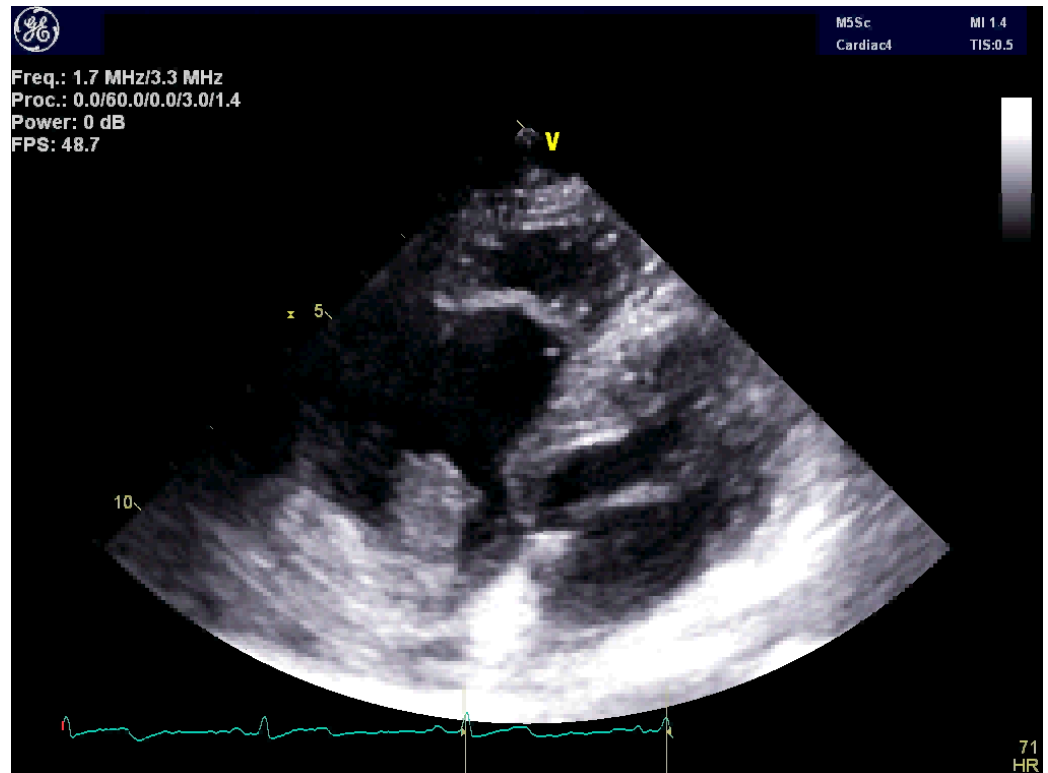
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## Case 3 – Cardiac Mass

- 32 year old female with left sided breast cancer. She is s/p doxorubicin (240 mg/m<sup>2</sup>), cytoxan and taxol and radiation therapy.
- Her echocardiogram reveals:

*How would you proceed?*

*Would you obtain additional imaging or other testing?*



# Common Primary Cardiac Masses of the Heart

## Benign

- Myxomas
- Fibroma
- Lipoma/Lipomatous hypertrophy of septum
- Thrombus
- Pericardial Cyst
- Papillary Fibroelastoma
- Rhabdomyomas (Pediatric)

## Malignant

- Sarcoma
- Lymphoma
- Thymoma
- Paraganglioma



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# Cardiac MRI Sequences

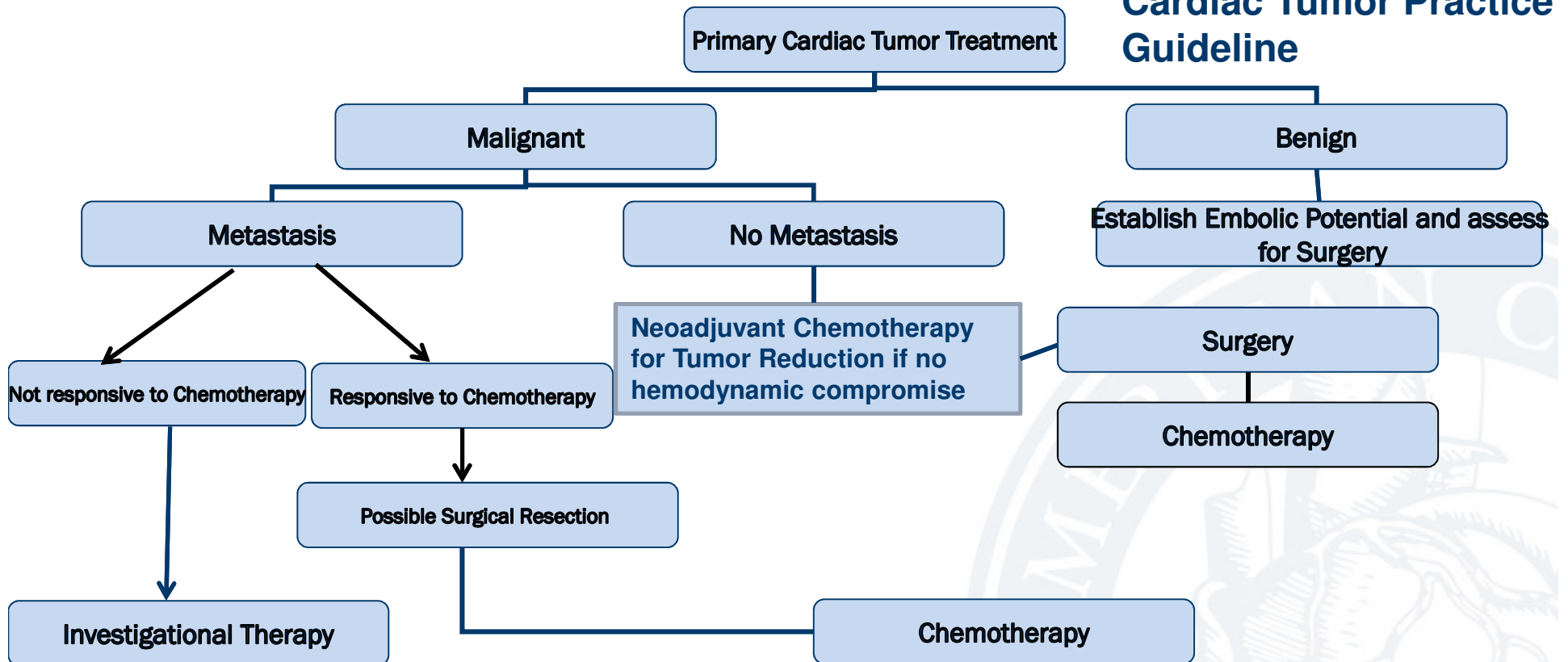
**Table 1.** CMR characteristics of cardiac masses

Cardic Mass	T1 Weighted	T2 Weighted	Post Contrast
Myxoma	Isointense, heterogeneous	Hyperintense, heterogeneous	Heterogeneous enhancement
Papillary fibroelastoma	Isointense	Hyperintense	Hyperintense
Rhabdomyoma	Iso- or hyperintense	Slightly hyperintense	Hyperintense
Fibroma	Iso- or hyperintense	Hypointense	Hyperintense
Hemangioma	Isointense	Hyperintense, heterogeneous	Hyperintense or heterogeneous
Paraganglioma	Iso- or hypointense	Hyperintense	Hyperintense
Intravenous leiomyomatosis	Isointense	Isointense	Heterogeneous
Bronchogenic cyst	Hypointense	Hyperintense	None
Angiosarcoma	Isointense, with hyperintense areas	Iso- or hyperintense	Hyperintense
Undifferentiated sarcoma	Isointense	Isointense	Nonspecific
Rhabdomyosarcoma	Isointense	Isointense, heterogeneous	Central nonenhancing areas
Osteosarcoma	Hyperintense	Hyperintense	Nonspecific
Malignant fibrous histiocytoma	Isointense	Hyperintense, heterogeneous	Nonspecific
Leiomyosarcoma	Isointense	Hyperintense	Nonspecific
Fibrosarcoma	Isointense, heterogeneous	Hyperintense	Central nonenhancing areas
Lymphoma	Hypo- or isointense	Hyperintense	Variable

Shah, DJ. Evaluation of Cardiac Masses: The Role of Cardiovascular MRI. Methodist DeBakey Cardiovascular Journal. 2010 Vol 6, No 3, 4-11.



# Cardiac Tumor Practice Guideline



## Case 3

*How would you proceed with anticoagulation? Coumadin? NOAC? Lovenox?  
And for how long?*



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## Case 4 – Cardio-Oncology Patients in the Cardiac Cath Lab

- **55 y/o WM 1.5 ppd smoker** for 30+ years with mild COPD on no treatment who presents with **h/o AML** and preoperative workup for allogeneic hematopoietic stem cell transplant.
- Has received 7 + 3 induction of **daunorubicin** and cytarabine. He is complaining of **mild chest pressure with stairs** and while shoveling snow for several months preceding his diagnosis.
- **Baseline ECG shows ischemic changes in V3-V6 with symmetrical T wave inversions.**

*How would you proceed?*



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## Case 4

- He undergoes a nuclear perfusion stress test with reversible ischemia in the mid to distal anterior wall consistent with LAD territory, EF 60%. Current labs include Hgb 10 and platelet count of 60,000.

*How would you proceed?*



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## Case 4

- Left heart catheterization shows mid 90% LAD lesion

*What next?*

*What is best antiplatelet regimen for this patient?*



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# Cardio-Oncology Patients In the Cardiac Catheterization Lab

- Chemotherapy agents may injure LV myocardium, cause endothelial damage, abnormal vasoreactivity, vasospasm, platelet activation and aggregation, progressive peripheral arterial disease
- Radiation therapies are also associated with premature CAD, constriction, restriction
- Diagnostic catheterization can be performed at any platelet level.
- ASA can be given with platelets > 10,000;  
Clopidogrel if platelets > 30,000  
Prasugrel or ticagrelor should not be given if platelets <50,000.



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## Useful References

- SCAI Expert Consensus Statement: Evaluation, Management, and Special Considerations of Cardio-Oncology Patients in the Cardiac Catheterization Lab. Catheter Cardiovasc Interv 2016; 87:E202-E223
- Iliescu, CA et al. Cardio-oncology patients in the cath lab. ACC.org Cardio-oncology Website (<http://www.acc.org/cardio-oncology>)
- Garot, et al. 2 Year Outcomes of High Bleeding Risk Patients After Polymer-Free Drug-Coated Stents. JACC. 2017; 69 (2): 162-71



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## Case 5 – Chest Pain Management with 5-FU

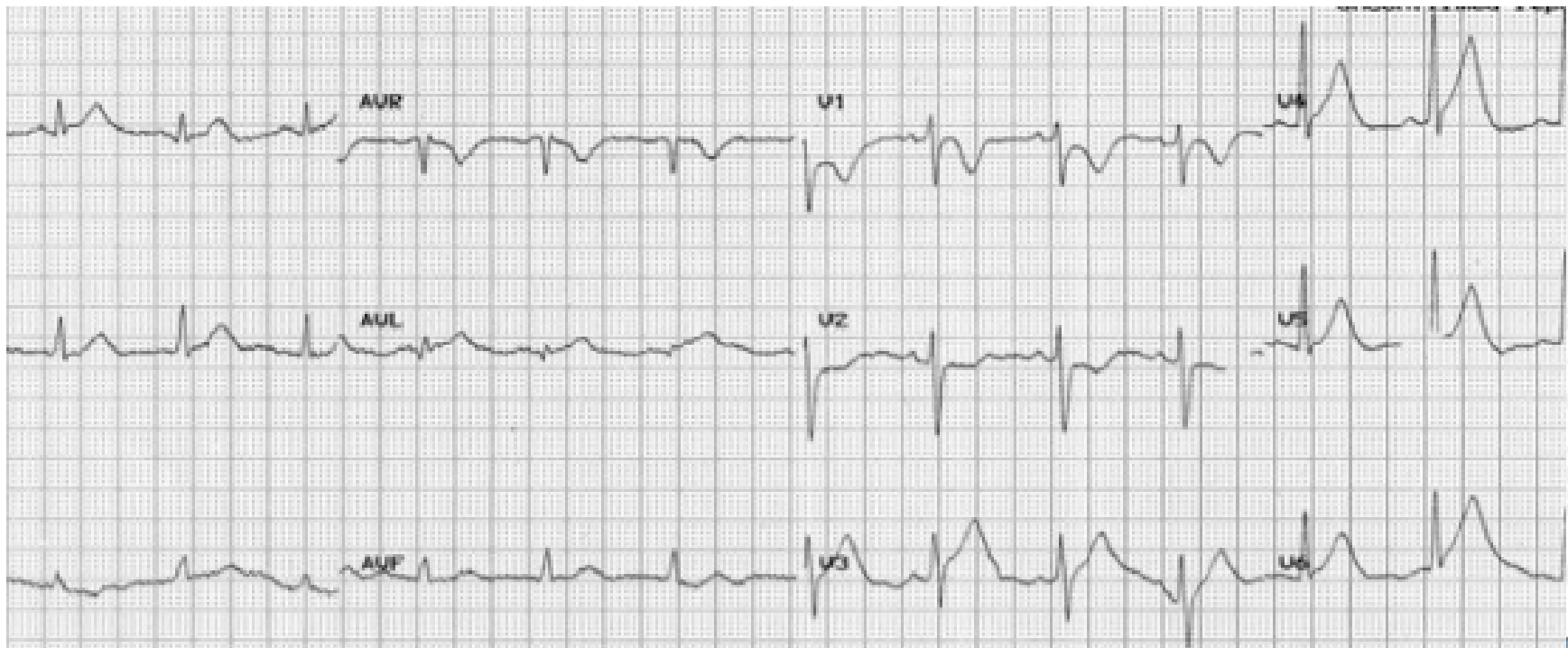
- **67 y/o WM** with **no significant PMH**, nonsmoker with **metastatic colorectal cancer** is being treated with **FOLFOX therapy** (Oxaliplatin 100 mg/m<sup>2</sup> IV infusion, given as a 120 minutes IV infusion in 500 mL D5W, concurrent with leucovorin 400 mg/m<sup>2</sup> IV infusion, followed by **5-FU 400 mg/m<sup>2</sup> IV bolus, followed by 46-hour 5-FU infusion (2400 mg/m<sup>2</sup>)**).
- On his second cycle, **after 1 hour of 5-FU infusion, the patient develops chest pain. Initial troponin I is 2.2 with CKMB 16.**

*What is your differential? How would you treat?*



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# ECG



Kim, S et al. The Korean Journal of Internal Medicine 2012; 27(3): 342-345



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## Case 5 – Chest Pain Management with 5-FU

- Echocardiogram shows hypokinetic anterior wall of the LV
- Left heart catheterization reveals nonobstructive coronary disease with all lesions noted to be less than 20%; this was performed within 24 hours of event
- Lipid panel: TC 240, LDL 135, HDL 38

*Would you give 5-FU again?*

*What other pharmacologic strategies would you use?*



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# 5-FU

- Antimetabolite that acts during S phase of cell cycle inhibiting DNA synthesis and interferes with RNA processing/function
- T1/2 10 minutes
- Liver Metabolism
- Manifestations: coronary vasospasm, ischemia/infarction, LV systolic dysfunction, arrhythmias (SVT, VT), sudden death
- Cardiotoxicity incidence 1.27 to 18%
- More often associated with infusion rather than bolus
- Bolus increases diarrhea, myelosuppression but some reports of less cardiotoxicity
- Calcium channel blockers, nitrates are often used



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