Cardio-Oncology

…in 30 mins or less!

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- General classes of chemotherapeutic agents
  - Anthracyclines
    - Doxorubicin (Adriamycin)
    - Epirubicin
  - Targeted therapy
    - HER2 receptor antagonists - Breast cancer; Esophageal cancer
    - VEGF receptor inhibitors - Solid tumors
    - Tyrosine kinase inhibitors - CML, ALL
    - Immune checkpoint inhibitors - Melanoma, Small cell CA
    - Androgen receptor inhibitors - Prostate CA

A 50-year-old female with invasive ductal carcinoma (ER+, PR+, HER2+) of the right breast and metastasis to an axillary lymph node presents to the Cardio-Oncology clinic to determine the most appropriate surveillance strategy for cardiac dysfunction while completing her therapy. Her staging scans were negative for distant metastasis. Her case was discussed at the breast cancer tumor board, and the patient elected to undergo lumpectomy with lymph node dissection. Neoadjuvant chemotherapy with doxorubicin and cyclophosphamide was recommended, followed by paclitaxel, trastuzumab, and pertuzumab (THP). She has completed the first part of the neoadjuvant regimen and has been started on THP. Which of the following is the recommended surveillance strategy for cardiac dysfunction in patients receiving trastuzumab?

A. Physical examination every month

B. Cardiac MRI every 6 months

C. Transthoracic echocardiogram every month while on trastuzumab

D. Transthoracic echocardiogram every 3 months while on trastuzumab

- The correct answer is D
  - Trastuzumab is a humanized monoclonal antibody with affinity for the HER2 receptor.
    - Meta-analysis of adjuvant Tras demonstrated significant reduction in mortality, recurrence, metastasis rates and second tutors other than Breast CA
    - Improves disease free survival by up to 50% when added to standard chemotherapy

- Echocardiography is recommended in following timeline
  - Pre-Anthracycline
  - Post-anthracyline, pre-trastuzumab
  - Every 3 months while on Trastuzumab
  - After completion of trastuzumab (often 1 yr post-anthracycline)
- Withhold trastuzumab
  - If LVEF drops > 10% to < 50%.
  - Start anti-HF medications: ACEi, beta-blockers, Spiro…
  - Re-assess LVEF in 4 weeks. IF back to normal, may resume trastuzumab
    - Re-assess LVEF 1 month after re-starting Trastuzumab

In which of the following clinical scenarios would reassessment of left ventricular function be recommended within 6 to 12 months after cancer treatment?

A. A 48-year-old female with essential hypertension and diabetes mellitus diagnosed with right-sided, triple-negative (ER–/PR–/HER2–) breast cancer treated with radical mastectomy and adjuvant anthracycline-containing chemotherapy (a cumulative dose of 240 mg/m^2 of doxorubicin)

B. A 59-year-old female diagnosed with ER+/PR+/HER2 negative, invasive ductal carcinoma of the right breast treated with radical mastectomy and adjuvant docetaxel and carboplatin, followed by maintenance endocrine therapy with an aromatase inhibitor

C. A 65-year-old male with essential hypertension and dyslipidemia who has relapsed multiple myeloma treated with carfilzomib for 6 months and is now in remission

D. A 56-year-old female with essential hypertension and obesity (body mass index: 32 kg/m^2) diagnosed with ER+/PR+/HER2–, invasive ductal carcinoma of the right breast treated with radical mastectomy, adjuvant radiation therapy to the right chest wall (total dose of 25 Gy), followed by maintenance endocrine therapy with tamoxifen

Patients at Increased Risk for Developing Cardiac Dysfunction due to Cancer Treatment
Treatment that includes any of the following: • High-dose anthracycline (e.g., doxorubicin at 250 mg/m^2, epirubicin at 600 mg/m^2) • High-dose radiotherapy (30 Gy) where the heart is in the treatment field • Lower-dose anthracycline (e.g., doxorubicin <250 mg/m^2, epirubicin <600 mg/m^2) in combination with lower-dose radiotherapy (<30 Gy) where the heart is in the treatment field
Treatment with lower-dose anthracycline (e.g., doxorubicin <250 mg/m^2, epirubicin <600 mg/m^2) or trastuzumab alone and the presence of any of the following risk factors: • Multiple CV risk factors (2 risk factors): smoking, hypertension, diabetes, dyslipidemia, and obesity during or after completion of therapy • Older age (60 years) at the time of cancer treatment • Compromised cardiac function (e.g., borderline reduced LVEF [50% to 55%], history of myocardial infarction, moderate valvular heart disease) at any time before or during treatment
Treatment with lower-dose anthracycline (e.g., doxorubicin <250 mg/m^2, epirubicin <600 mg/m^2), followed by trastuzumab (sequential therapy)

Which of the following is characteristic of radiation-associated coronary artery disease?

A. Usually clinically manifests days to weeks post radiation exposure

B. Typically involves the distal aspects of the epicardial coronary arteries and microvascular bed

C. Can be rapidly progressive

D. Mortality rates are lower in patients requiring coronary artery bypass grafting (CABG) compared to the general population given the younger age of the patients.

Which of the following is a characteristic echocardiographic finding associated with chest radiation?

A. Pulmonic valve stenosis

B. Apical ballooning

C. McConnell's sign

D. Thickening and calcification of the aorto-mitral curtain

- The correct answer is C
- Radiation-associated coronary artery disease has a long latent period, manifesting years to decades after radiation exposure. It can be rapidly progressive and typically affects the ostia or proximal aspects of the epicardial coronary arteries likely related to the vessel position within the anterior radiation field.
- Morbidity and mortality associated with surgical revascularization is higher in irradiated patients when compared with those without radiation exposure due to high prevalence of multivessel disease, associated valvular disease, calcific aorta and mediastinal pathology and decreased cardio-pulmonary reserve.

A 55-year-old female presents to the Cardio-Oncology clinic complaining of worsening shortness of breath and lower extremity edema. She has history of Hodgkin lymphoma at the age of 15 years for which she received mantle radiation. She does not remember the total dose of radiation and receiving chemotherapy. She has gained about 15 pounds (7 kilograms) over the past 2 weeks. Physical examination revealed 2+ bilateral lower extremity pitting edema extending up to the knees, elevated jugular venous pressure with lack of inspiratory decline, pulsatile liver, and ascites. Vital signs include heart rate 102 beats per minute, blood pressure 100/60 mmHg, respiratory rate 14 breaths per minute, and 97% oxygen saturation on room air. A transthoracic echocardiogram showed a normal LVEF and no gross valvular abnormality; however, no further evaluation could be performed due to suboptimal image quality.

What is the most appropriate next step?

A. Coronary CT angiography

B. Myocardial perfusion scan

C. Right and left heart catheterization

D. Endomyocardial biopsy

What is the most likely diagnosis?

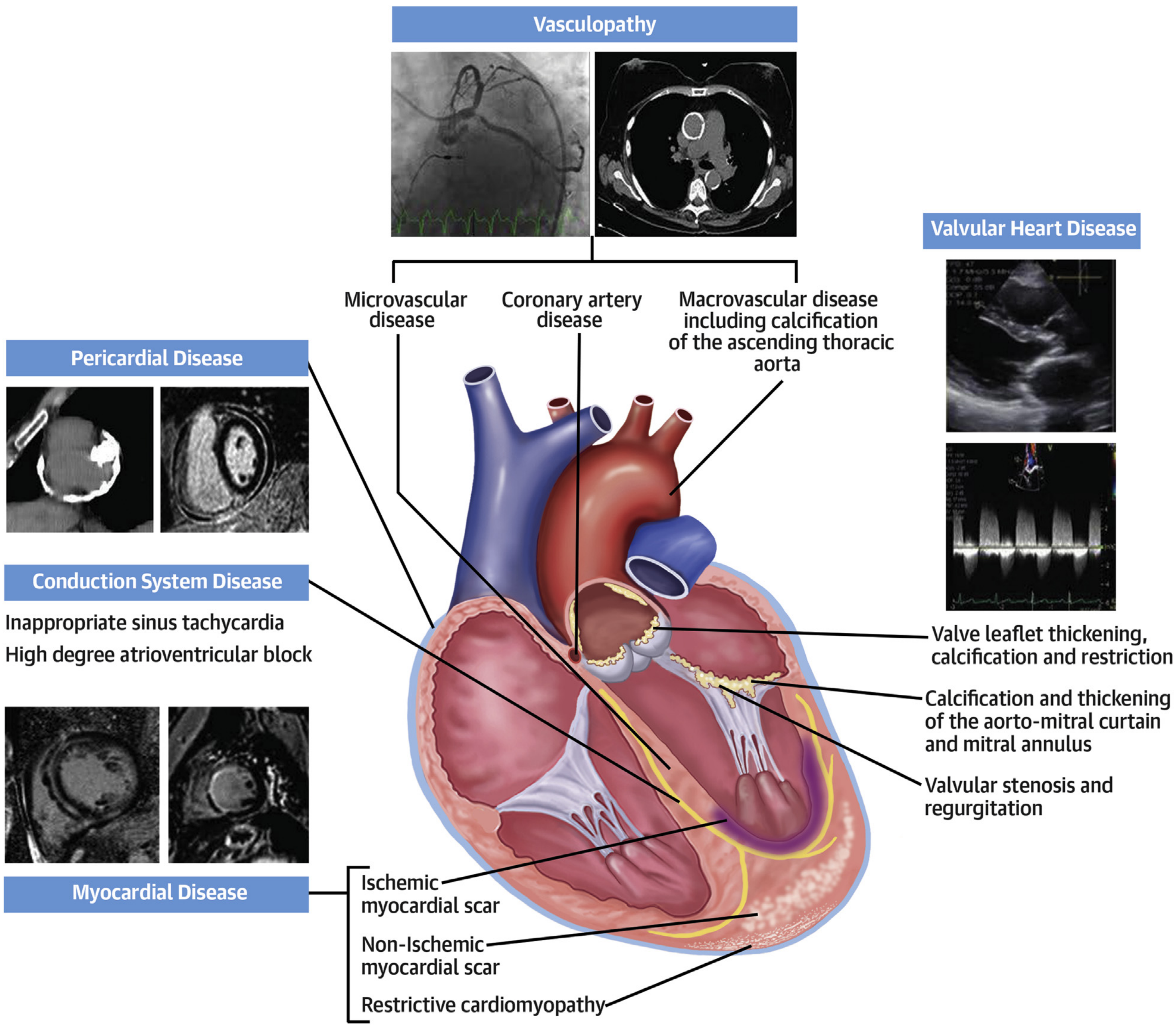
A. Radiation-induced coronary artery disease

B. Constrictive pericarditis

C. Acute myocarditis

D. Acute pulmonary embolism

CENTRAL ILLUSTRATION Various Manifestations of Radiation-Associated Cardiac Disease



Desai, M.Y. et al. J Am Coll Cardiol. 2019;74(7):905–27.

A 65-year-old male with history of paroxysmal atrial fibrillation presents with 3 months of progressive lower extremity edema and shortness of breath. Laboratory tests showed a serum creatinine 2.4 mg/dL (212.2 mol/L) and hemoglobin 12.6 g/dL (7.82 mol/L). Proteinuria is present on urinalysis. ECG shows diffuse low QRS voltage. What is the next best step in the diagnostic evaluation?

A. NT-proBNP, troponin, and cardiac MRI

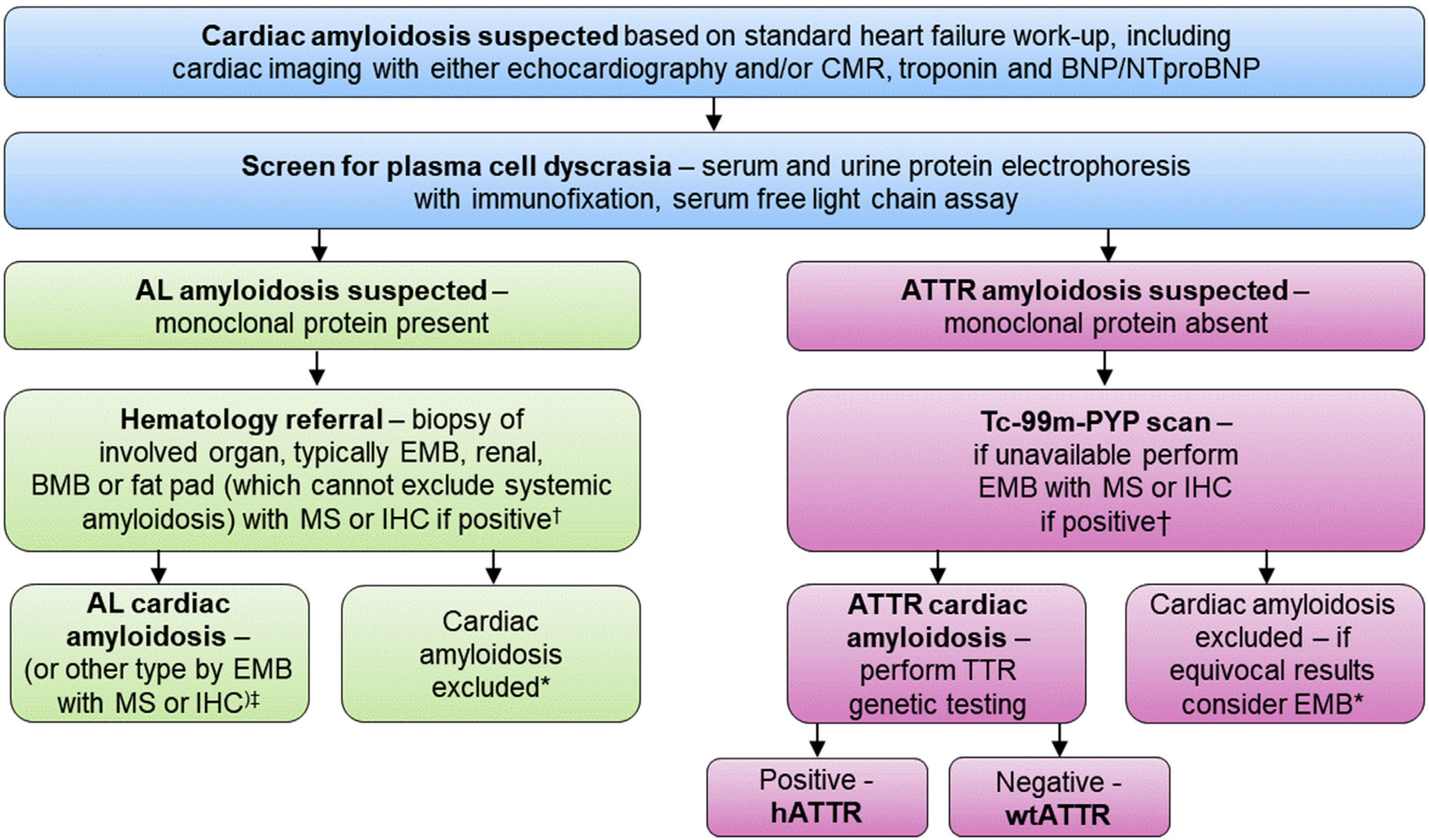
B. Serum and urine protein immunofixation, serum free light chains, NT-proBNP, troponin, and transthoracic echocardiogram

C. Serum and urine protein immunofixation, 24-hour urine level, NT-proBNP, troponin

D. Transthyretin genetic testing

- The correct answer is B.

    - The clinical history, renal function abnormalities, and ECG findings are suggestive of an infiltrative cardiomyopathy, specifically cardiac amyloidosis. Other findings associated with amyloidosis include heart failure, bilateral carpal tunnel syndrome, lumbar spinal stenosis, biceps tendon rupture, atrial arrhythmias or conduction disease, and echocardiographic findings suggestive of an infiltrative cardiomyopathy, including apical sparing on strain imaging.



Cardiac amyloidosis suspected based on standard heart failure work-up, including cardiac imaging with either echocardiography and/or CMR, troponin and BNP/NTproBNP
Screen for plasma cell dyscrasia – serum and urine protein electrophoresis with immunofixation, serum free light chain assay
AL amyloidosis suspected – monoclonal protein present
ATTR amyloidosis suspected – monoclonal protein absent
Hematology referral – biopsy of involved organ, typically EMB, renal, BMB or fat pad (which cannot exclude systemic amyloidosis) with MS or IHC if positive†
Tc-99m-PYP scan – if unavailable perform EMB with MS or IHC if positive†
AL cardiac amyloidosis – (or other type by EMB with MS or IHC)‡
Cardiac amyloidosis excluded*
ATTR cardiac amyloidosis – perform TTR genetic testing
Cardiac amyloidosis excluded – if equivocal results consider EMB*
Positive - hATTR
Negative - wtATTR

A 76-year-old male was referred to the Cardio-Oncology clinic for evaluation for palpitations. He has essential hypertension, type 2 diabetes mellitus, and relapsed chronic lymphocytic leukemia (CLL). He has been on ibrutinib for 2 years. He has symptoms of mild exercise intolerance and the sense of an irregular heartbeat. He denies having near syncope, syncope, orthopnea, shortness of breath, or chest pain. Vital signs include temperature 98.6°F (37°C), heart rate 120 beats per minute, blood pressure 148/82 mmHg, and respiratory rate 14 breaths per minute. Physical exam revealed an irregularly irregular heart rhythm. An ECG demonstrated atrial fibrillation with rapid ventricular response (116 beats per minute). What is the best initial rate- or rhythm-control strategy?

A. Rate control with diltiazem

B. Rate control with metoprolol

C. Rhythm control with amiodarone

D. Immediate direct-current cardioversion

- The correct answer is B.
    - Ibrutinib is a Bruton tyrosine kinase inhibitor approved to treat CLL, Waldenstrom's macroglobulinemia, and marginal cell lymphoma
    - CV adverse effects include atrial fibrillation, hypertension and ventricular arrhythmias.
    - Best initial approach is rate control with a beta-blocker
    - Ca-channel blockers are contraindicated due to CYP450 interaction
    - Cardioversion if patient is unstable
- **Know that Ibrutnib is associated with atrial fibrillation, treated with beta-blockers and avoid DOACs with CYP 450 activity**

A 62-year-old male underwent a bone marrow biopsy confirming the diagnosis of BCR-ABL positive, chronic myeloid leukemia (CML) in chronic phase. His past medical history includes hypertension, type 2 diabetes, and coronary artery disease with percutaneous coronary intervention to the mid left anterior descending artery five years ago. The oncologist discussed the prognosis and treatment with the patient, and the plan is to start dasatinib. Which of the following is a known CV adverse effect from dasatinib?

A. Atrial fibrillation

B. Ventricular tachycardia

C. Pleural effusion

D. Stroke

- The correct answer is C.
- Small molecule Tyrosine Kinase Inhibitors
  - Imatinib
  - Dasatinib
  - Nilotinib
  - Ponatinib

- Cardiac adverse effects include
  - **Systemic Hypertension**
  - Venous and arterial thromboembolic disease
  - Pleural effusion and pulmonary hypertension
  - Dyslipidemia and hyperglycemia