Clinical Oncology: Case Reports

Case Report

A SCITECHNOL JOURNAL

Cardiac Risk Stratification in Bone Marrow Transplant Recipients with Myelodysplastic Syndrome: The Role of Multimodal Imaging

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Abstract

Multimodal imaging techniques have significantly enhanced our understanding and management of cardiovascular diseases. Some of the methods include echocardiography, Myocardial Perfusion Imaging (MPI), Cardiac Computed Tomography (CCT), Cardiac Magnetic Resonance Imaging (CMR), and nuclear cardiology Single Photon Emission Computed Tomography (SPECT) and Positron Emission Tomography (PET). These methods are frequently combined to detect high-risk cardiovascular comorbidities in both symptomatic and asymptomatic individuals, enabling prompt interventions that positively impact overall survival. We present the case of a 74-years-old male with Myelodysplastic Syndrome (MDS) who underwent comprehensive cardiovascular risk assessment before Hematopoietic Stem Cell Transplantation (HSCT), revealing significant coronary artery disease alongside his comorbidities and risk factors. His initial evaluation with Transthoracic Echocardiography (TTE) showed normal overall Left Ventricular (LV) peak systolic average Global Longitudinal Strain (GLS) and Left Ventricular Ejection Fraction (LVEF). At the same time, MPI revealed no significant reversible ischemia and a normal LVEF by quantitative assessment, indicating low cardiovascular risk based on the interpretation of these results. However, the TTE image review by the clinician revealed LV regional strain abnormalities and the MPI review noted upper-normal Transient Ischemic Dilatation (TID) with an associated inferior predominantly fixed defect. Pre-HSCT surveillance Computed Tomography (CT) image review also incidentally revealed extensive coronary artery calcification. Cardiac catheterization confirmed triple vessel Coronary Artery Disease (CAD), and the patient subsequently underwent Coronary Artery Bypass Grafting (CABG) to mitigate cardiovascular risk and optimize health post-HSCT. This case highlights the critical role of multimodal cardiac imaging in cardiovascular risk stratification for patients undergoing HSCT, emphasizing the need for clinicians to incorporate all available imaging techniques to improve cardiovascular outcomes in this patient population.

Keywords: Coronary Artery Bypass Grafting (CABG); Cardiac imaging; Left Ventricular (LV); Echocardiography; Computed Tomography (CT); Cardiotoxicity

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Received: Nov 11, 2024; Manuscript No: COCR-24-152621 **Editor Assigned:** Nov 17, 2024; PreQC Id: COCR-24-152621 (PQ) **Reviewed:** Nov 20, 2024; QC No: COCR-24-152621 (Q) **Revised:** Nov 25, 2024; Manuscript No: COCR-24-152621 (R) **Published:** Nov 29, 2024; DOI: 10.4173/cocr.7(11).359

Introduction

Hematopoietic stem cell transplantation can be a potential cure for various disorders including myelodysplastic syndrome but poses cardiovascular risks, especially for elderly patients and those with an associated cardiovascular disease. In adults, arrhythmias such as atrial fibrillation and flutter are the most frequent acute cardiovascular complications. Acute heart failure has an incidence ranging from 0.4% to 2.2% [1]. Comorbidities, including hypertension, chronic kidney disease, coronary artery disease, and heart failure, are important risk factors for developing short and long-term cardiovascular complications [2]. High-risk cardiovascular conditions with compromised cardiac reserve, including advanced heart failure, untreated severe valvular heart disease, and significant triple-vessel or left main obstructive coronary artery disease, are linked to unfavorable outcomes (1-year survival rates of 30%-50%), irrespective of Hematopoietic Stem Cell Transplantation (HSCT). These conditions generally contraindicate candidacy for HSCT unless a corrective intervention can be performed before transplantation. Consequently, a comprehensive pretransplant evaluation must prioritize the identification of high-risk cardiovascular disease, employing a thorough clinical history, physical examination, and appropriate diagnostic testing [3]. This case involves a 74-years-old male with Myelodysplastic Syndromes (MDS) and significant cardiovascular risk factors who required multimodal cardiac diagnostic imaging to accurately diagnose triple-vessel coronary artery disease, highlighting his increased risk for complications post-Hematopoietic Stem Cell Transplantation (HSCT), such as cardiac arrhythmias, myocardial infarction, and heart failure.

Case Presentation

A 74-years-old African American male with a medical history significant for Myelodysplastic Syndrome (MDS), hypertension, hyperlipidemia, emphysema, goiter, Obstructive Sleep Apnea (OSA), and Diabetes Mellitus (DM) Type II on insulin and oral agents presented to the cardio- oncology clinic for cardiovascular risk assessment before HSCT.

His diagnosis of MDS included positive mutations for BCOR, RUNX1, and SF3B1, which categorize him as intermediate risk. The patient had experienced progressive anemia that had proven refractory to erythropoiesis-stimulating agents, including Procrit and Luspatercept, and was being treated with azacitidine at the time of evaluation. Despite the therapy, he remained transfusion-dependent for red blood cells and platelets.

The patient did not have any symptoms like chest pain, palpitations, dyspnea, orthopnea, paroxysmal nocturnal dyspnea, lower extremity edema, dizziness, or syncope.

A Transthoracic Echocardiogram (TTE) revealed a normal left ventricular cavity size, mild concentric left ventricular hypertrophy, normal wall motion, and systolic function with an ejection fraction of 55%-60%. Diastolic function was also assessed as normal, with a triplane peak systolic average endocardial global longitudinal strain of -18.50% (Figure 1). Additionally, right ventricular systolic function and wall thickness were normal, though there was mild mitral annular calcification with mild regurgitation, and the pulmonary artery systolic pressure was measured at 25 mmHg.

A nuclear pharmacological stress test yielded a calculated ejection fraction of 64%. A small predominantly fixed defect with moderately reduced activity was noted in the apical inferior and apex walls, which was attributed to diaphragmatic attenuation, with overall normal wall motion and no evidence of ischemia. Transient ischemic dilatation at a value of 1.3 which is at upper normal for rest stress regadenoson myocardial perfusion imaging (Figure 2).

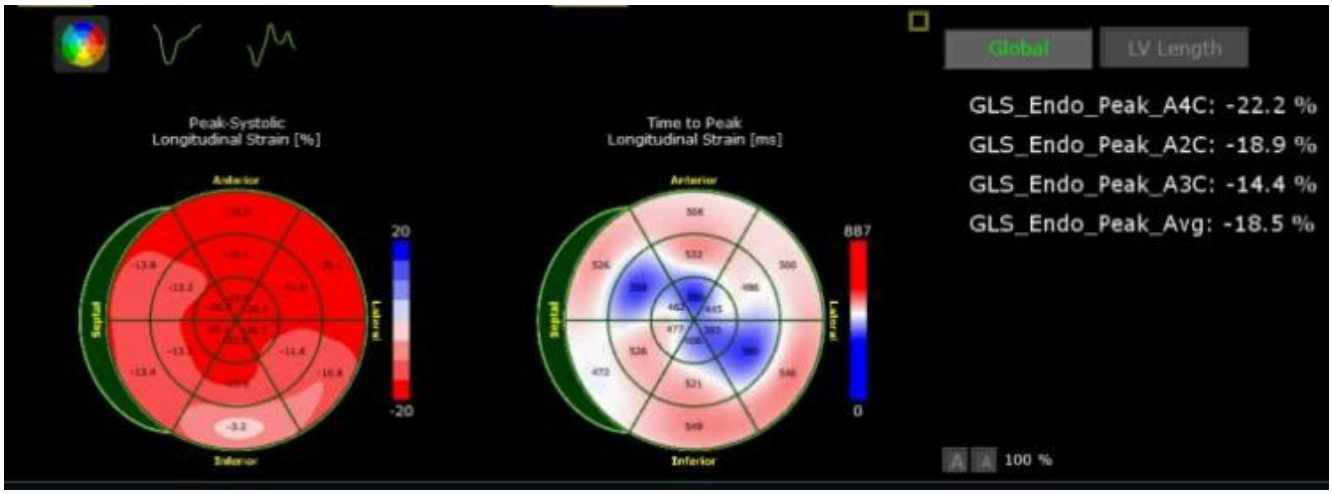

Figure 1: TTE Bull's eye strain imaging with a normal triplane endocardial peak systolic average global longitudinal strain of -18.50% but with a regional strain abnormality.

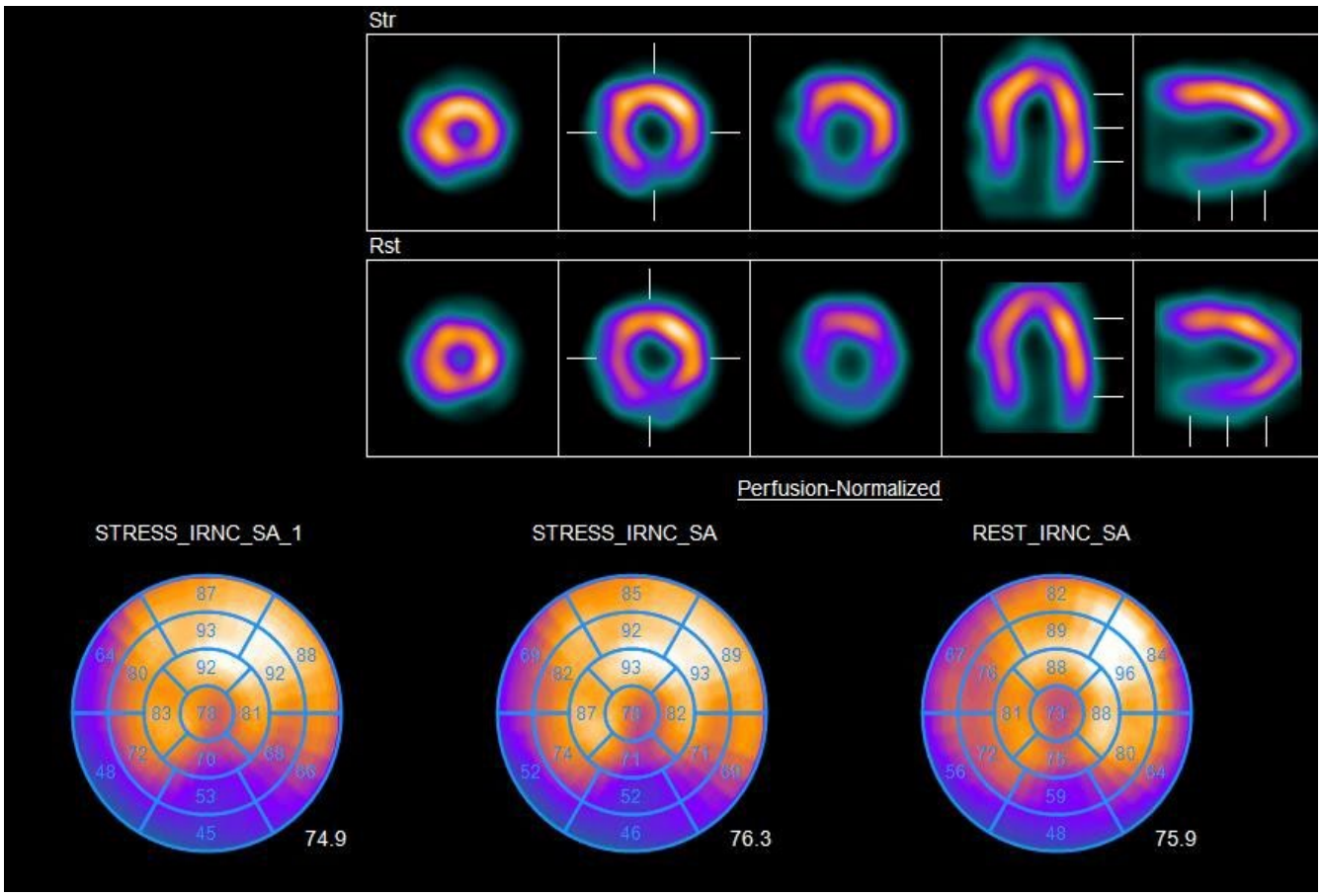

Figure 2: MPI showing a small predominantly fixed defect with moderately reduced activity in the apical inferior and apex walls.

A retrospective review of a previously performed contrast-enhanced CT of the chest revealed extensive coronary calcification involving the Right Coronary Artery (RCA), Left Anterior Descending coronary Artery (LAD) and Left Circumflex Coronary Artery (LCX) (Figures 3 and 4).

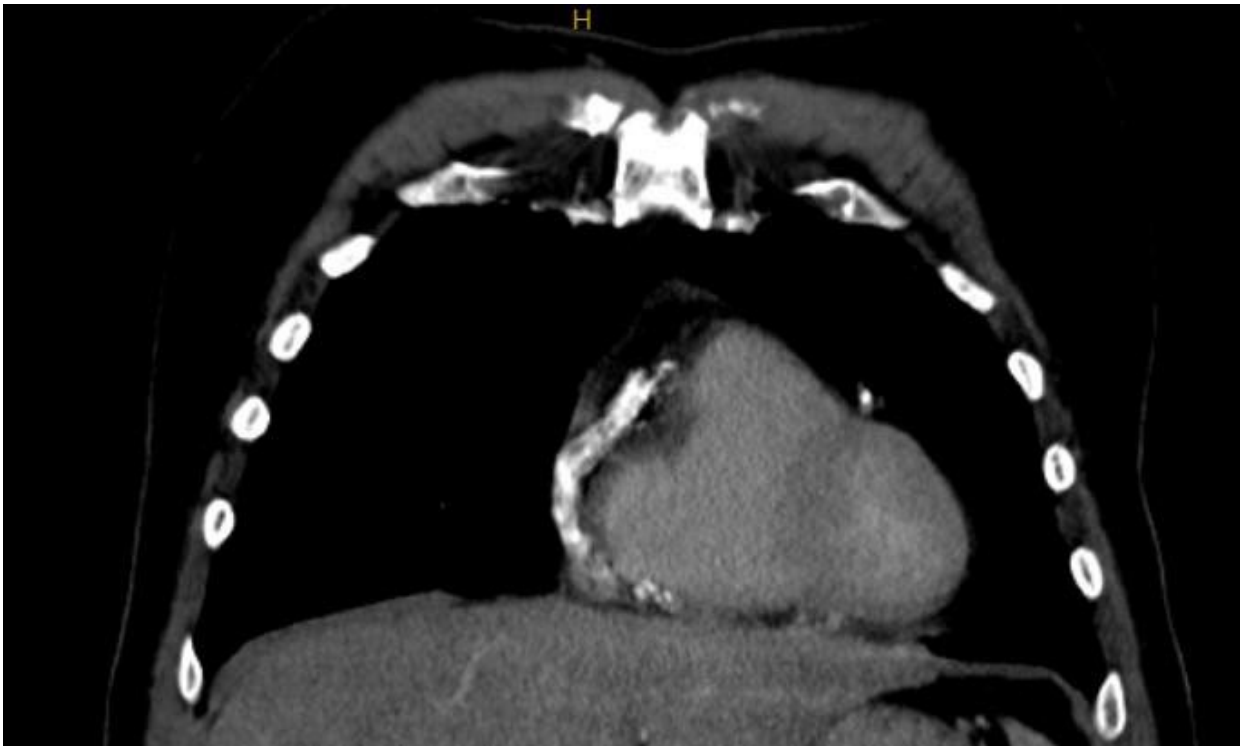

Figure 3: CT showing RCA calcification.

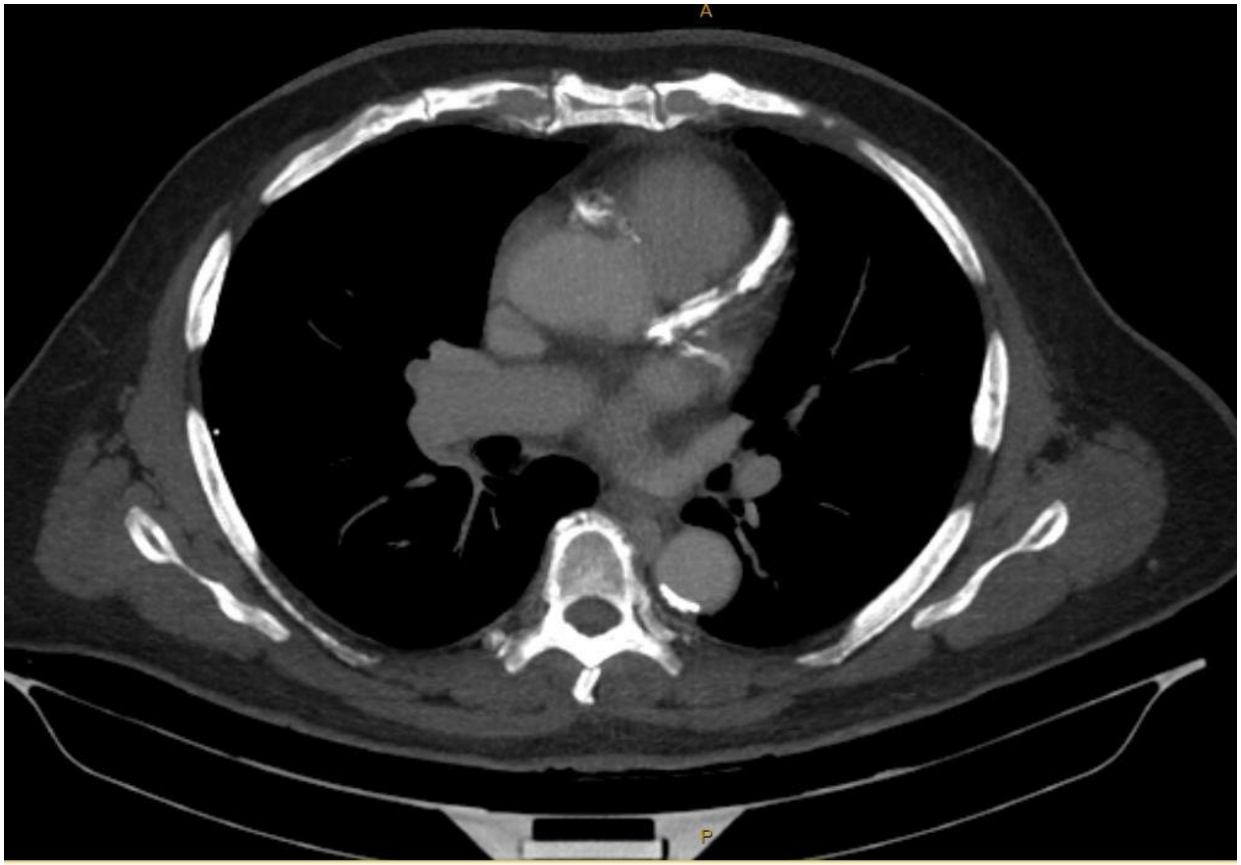

Figure 4: CT showing LAD calcification.

Given the extensive calcification of coronary arteries, the findings from the nuclear stress imaging study, and the abnormal regional strain imaging by the TTE study, the likelihood of underlying coronary artery disease was considered as a potential high risk predisposing factor for a potential cardiovascular event after HSCT, prompting cardiac catheterization for further evaluation.

During cardiac catheterization, a 60% distal lesion was identified in the left main coronary artery, extending to the bifurcation of the LAD and LCX. In the LAD, an 80% lesion was found in the mid segment and a 70% lesion in the distal segment, with severe calcification observed. Additionally, an 80% lesion was noted in the proximal segment of the obtuse marginal branch, while the RCA exhibited a 95% lesion in the mid to distal segments and a subtotal occlusion in the posterior left ventricular branch.

Due to the extensive coronary artery disease, the patient was classified as a high-risk candidate for HSCT without pre-procedural optimization and was therefore referred for Coronary Artery Bypass Grafting (CABG). The patient underwent a 4-vessel CABG. Following the surgery, the plan, as discussed among the Cardio-Oncology team, along with the Cardiothoracic Surgery (CTS), Bone Marrow Transplant (BMT), and oncology multidisciplinary teams, was to re-stratify the patient's cardiovascular risk two months post-CABG. At that time, the patient would be reassessed for HSCT, now with a reduced risk for cardiovascular complications compared to the initial Cardio-Oncology assessment.

Discussion

Hematopoietic Stem Cell transplantation (HSCT) is a well-established treatment modality for various hematological disorders and malignancies, significantly improved over the last five decades to enhance long-term survival rates. Currently, there are approximately 250,000 HCT survivors in the United States, a figure expected to double in the next decade. Despite these advancements, HCT survivors face significantly higher mortality rates compared to the general population, with cardiovascular-related mortality more than double that of the general population and increasing over time following transplantation (Chang et al., 2019) [6]. They experience increased cardiovascular death with an adjusted incidence rate difference of 3.6 per 1000 person-years. They also have an increased cumulative incidence of ischemic heart disease, cardiomyopathy or heart failure, stroke, vascular diseases, and rhythm disorders [2-8].

Mechanisms of cardiac complication

Some of the mechanisms of cardiac complications include direct endothelial injury related to the conditioning regimen, the acute hyperinflammatory state secondary to engraftment syndrome, and chronic inflammation in Graft Versus Host Disease (GVHD) [9].

Risk factors for adverse cardiovascular outcomes

In a study published by Vasbinder et al., Multiple risk factors were attributed to adverse cardiovascular outcomes after HSCT. Patients with the following characteristics were found to have greater incidence of cardiovascular events after HSCT. Older patients (mean age, 59 *vs.* 54 years), more likely to have had an allogeneic transplant (51.1% *vs.* 43.5%), men (66.4% *vs.* 58.6%), have a body mass index >25 kg/m^2 (80.7% versus 73.4%), more likely to have ahistory of hypertension (55.9% *vs.* 43.3%), chronic kidney disease (9.0% *vs.* 5.3%), coronary artery disease (22.8% *vs.* 10.7%), heart failure (7.2% versus 3.6%), and peripheral artery disease (3.9% *vs.* 1.4%), and have higher average pre-HSCT creatinine (mean 0.96 *vs.* 0.85 mg/dL) and triglycerides (211 versus 194 mg/dL) compared with HSCT recipients who did not de-velop cardiovascular events. (Vasbinder et al., 2023) [2].

Pre HSCT cardiac evaluations

American Heart Association recommends four steps in pre-HSCT evaluation [9]:

Initial risk stratification

Exclusion of high-risk cardiovascular disease

Assessment of cardiac reserve

Optimization of cardiovascular reserve

Initial risk stratification can be done by careful history taking, detailed physical examination, assessing functional status of the patient, utilizing multimodal imaging and using scoring tools like CARE-BMT risk score.

Most critical step in pre-HSCT is to exclude the presence of high-risk cardiovascular comorbidities such as advanced heart failure, severe valvular heart disease, and severe triple vessel or left main obstructive coronary artery diseases. Some of the diagnostic modalities include Transthoracic Echocardiography (TTE), Transesophageal Echocardiography (TEE), Myocardial Stress Perfusion Imaging (MPI), Coronary Computed Tomography Angiography (CCTA), Cardiac Magnetic Resonance Imaging CMRI), and Cardiac catheterization.

University of Michigan Cardiovascular Registry in Bone Marrow Transplantation (CARE-BMT) risk score is a simple, easy to calculate, pre-hematopoietic stem cell transplant risk score to identify patients at high risk of developing cardiovascular events after transplant. This score could be used during pretransplant evaluations to guide referrals of high-risk transplant recipients to cardiovascular specialists (Tables 1 and 2).

Table 1: CARE-BMT risk score point assignment.

Variables	Points
Age(years) 50-54	1
Age(years) 55-64	2
Age(years) 65 or greater	3
Black Race	1
Allogeneic HSCT	2
Anthracycline >250 mg/m²	2
Coronary artery disease	1
Heart failure	1
Peripheral artery disease	1
Serum creatinine >1 mg/dL	1
Triglyceride >150 mg/dL	1

Table 2: Interpretation of total CARE-BMT risk score.

Total Score	Score	Risk Group	1-Year Incidence of CV Event	5-Years Incidence of CV Event
0-16 points	0-1 point	Low-risk	1.70%	4.00%
	2-4 points	Intermediate- risk	4.00%	10.30%
	≥ 5 points	High-risk	11.30%	22.40%

Cardiac reserve means the ability of the cardiovascular system to overcome the stress response secondary to HSCT. Some of the stresses include direct cardiotoxicity, rapid volume shifts, increased oxygen demand due to anemia, and the systemic inflammatory response. Cardiac reserve can be predicted by detailed history to identify presence of risk factors and pertinent findings on physical examination. Presence of Jugular Venous Distension (JVD), poor exercise tolerance, Maximum Oxygen Consumption (MOC) during cardiopulmonary stress test, Metabolic Equivalents (MET) and six-minute walk tests are some of the objective ways to predict cardiac reserve in the patients. Treating reversible cardiovascular diseases, optimizing volume status, managing blood pressure, using guideline based medical therapy to maximum tolerated amounts are some of the ways to improve cardiac reserve (Table 3).

Table 3: Diagnostic performance of different imaging techniques to detect hemodynamically significant coronary artery disease [10].

Tests	Sensitivity	Specificity	PLR	NLR
CCTA	0.9	0.39	1.54	0.22
SE	0.77	0.75	3	0.34
ICA	0.69	0.67	2.54	0.46
CMRI	0.9	0.94	10.31	0.12
SPECT	0.7	0.78	3.4	0.4

CCTA: Coronary Computed Tomography Angiography, SE: Stress Echocardiography, ICA: Invasive Coronary Angiography, CMRI: Cardiac Magnetic Resonance Imaging, SPECT: Single-Photon Emission Computed Tomography, PLR: Positive Likelihood Ratio, NLR: Negative Likelihood Ratio.

Reflecting to the case

TTE image review by the clinician revealed LV regional strain abnormalities, consistent with findings from Norum et al. (2022), which highlight the utility of regional longitudinal strain by speckle tracking to detect significant coronary artery disease even in patients with normal overall average GLS and LVEF [4]. The MPI review noted upper-normal Transient Ischemic Dilatation (TID). As observed in our patient, TID serves as an independent and incremental prognostic marker for cardiac events, even after adjusting for significant clinical variables. Other studies also indicate that stress- induced left ventricular dilation is an independent marker of increased risk, even without perfusion abnormalities [5-7].

Conclusion

Cardiac dysfunction is a significant adverse effect of certain cancer therapies, potentially compromising treatment efficacy, reducing quality of life, and impacting overall survival in cancer patients. Oncologists and advanced care practitioners should address the risk of cardiac dysfunction in high-risk individuals prior to initiating therapy. Although discussing potential complications early in the cancer journey may be challenging for patients who are primarily focused on cancer survival, clear communication between providers and patients is essential for effective monitoring and the implementation of preventive strategies. A thorough baseline cardiac risk assessment should be conducted before treatment, and a detailed, individualized plan for cardiac monitoring during and after therapy is crucial for high-risk patients. Appropriate pre-HSCT interventions should be discussed with the patient, the oncology team, and the HSCT team to implement measures that reduce post-HSCT survivorship risks and improve cardiovascular outcomes. Furthermore, patients should be made aware that cardiac dysfunction can be progressive and may be asymptomatic in its early stages, highlighting the importance of recognizing and reporting early and late signs to their oncology team or a cardiologist.

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