Integrating Biomarkers into Oncology: A New Era in Cardiotoxicity Monitoring

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Abstract

Cancer and cardiovascular disease are the leading causes of mortality worldwide, and advancements in cancer therapy have significantly improved patient survival. However, many anticancer treatments including chemotherapy, radiotherapy, targeted therapies, and immune checkpoint inhibitors are associated with a wide range of cardiovascular toxicities such as heart failure, coronary artery disease, myocarditis, arrhythmias, and venous thromboembolism. Biomarkers have emerged as valuable tools in the diagnosis, risk stratification, and monitoring of cardiovascular disease in cancer patients. Established biomarkers such as cardiac troponins and natriuretic peptides (BNP and NT-proBNP) play a key role in identifying myocardial injury and cardiac dysfunction. Additionally, D-dimer is widely used in the assessment of thrombotic risk. This review summarizes the current understanding of cardiovascular biomarkers in the context of cancer therapy-induced cardiotoxicity, highlighting their role in heart failure, acute coronary syndromes, myocarditis, and venous thromboembolism.

Keywords: Biomarkers; Cancer; Cardiovascular; Myocarditis; Thromboembolism;

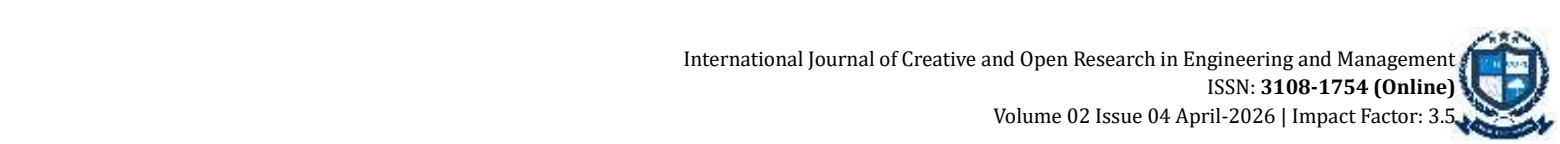
1. Introduction

Cancer and cardiovascular (CV) disease continue to be the two leading causes of death in Western populations. Substantial progress in cancer treatment has significantly prolonged long-term survival of cancer patients in the past several decades [1]. Cardiac dysfunction due to cancer therapy preventable with treatments whether traditional or new, cancer treatments have promised, and delivered on, life and limb, though an unprecedented milieu of cardiotoxicity. These CV adverse effects could be attributed to radiotherapy, cytotoxic agents as well as to the newer modalities, that is, molecularly targeted therapies and immune checkpoint inhibitors. The clinical presentations are of heart failure, CAD, ACS, myocarditis, VTE, valvular defects, and arrhythmias [2]. Cardiac toxicity associated with cancer treatment is considered particularly unpredictable with the advent of new therapeutic tools. Cardio-oncology branch of medicine aimed at enhancing better evaluation, diagnosis and treatment of cancer treatment-induced cardiovascular complications. Tailored diagnostic pathways are necessary for optimal risk stratification, patient management, and long-term follow-up. Despite the fact that biomarkers are commonly used in the diagnosis of acute and chronic cardiac diseases, the early detection and monitoring of CTIC based on biomarkers is to date not well established and seems to be more complex than in primary cardiovascular disease [3]. The aim of this review is to summarize the present knowledge, clinical implication, and future direction of the use of the biomarkers for diagnosis and management of cardiovascular side effects of cancer treatment.

2. Biomarkers in Cardiovascular Risk Assessment

Biomarkers play a crucial role in the diagnosis and treatment of cardiovascular diseases. Brain natriuretic peptide (BNP) and its N-terminal pro-BNP (NT-proBNP) are established biomarkers for heart failure (HF) diagnosis [4]. BNP is synthesized and secreted by heart muscle cells in response to elevated transmural pressure or activation of neurohumoral pathways, both of which are influenced by noradrenaline and angiotensin II . Synthesized initially as preproBNP, it is subject to proteolysis of a 25-amino acid peptide to become proBNP and is stored in intracellular vesicles [5]. Once activated, proBNP is cleaved into active BNP and inactive NT-proBNP. Peptides are released in equimolar amounts, with BNP having a half-life of about 20 min and NT-proBNP a much longer half-life of around 120 min, resulting in circulating NT-proBNP levels being maintained at 4 to 6-fold greater concentrations than BNP. BNP is bioactive and has an important role in reducing cardiac preload and afterload by elevation of glomerular filtration rate (GFR) and vasodilation [6]. Furthermore, BNP also stands in as an inhibitor of deleterious myocardial remodeling, acting in opposition to the maladaptive neurohumoral systems of heart failure. Both BNP and NT-proBNP are very sensitive indices of heart failure, but lack specificity for diagnosis. The lower diagnostic cutoff for BNP is 35 ng/mL, while for NT-proBNP it is 125 ng/mL, with negative predictive values for heart failure ranging from 0.94 to 0.98 and positive predictive values ranging from 0.44 to 0.57. According to the guidelines of the European Society of Cardiology (ESC) and the American Heart Association (AHA), measurement of BNP/NT-proBNP is considered a key diagnostic criterion for heart failure. Moreover, BNP screening in individuals at risk of heart failure may be valuable for early intervention to prevent disease progression. The role of BNP/NT-proBNP in guiding therapy for patients with established heart failure remains a topic of debate [7].

Various conditions, especially renal failure, can result in elevated levels of natriuretic peptides. BNP and NT-proBNP are cleared from the plasma via different mechanisms. BNP binds to its receptors, where it is either cleaved by an endopeptidase or excreted through the kidneys. In contrast, NT-proBNP is completely excreted by the kidneys [8]. Although both peptides are elevated in renal insufficiency, the ratio of NT-proBNP to BNP inversely correlates with the estimated glomerular filtration rate (GFR). As a result, BNP and NT-proBNP levels must always be interpreted with consideration of the patient's renal function as indicated by GFR. Additionally, factors such as age, female sex, hypertension, atrial fibrillation, and diabetes mellitus are associated with higher BNP/NT-proBNP levels [9]. In cancer patients and those undergoing cancer therapy, anemia and fluid status are particularly influential in affecting natriuretic peptide concentrations. Interestingly, obesity is linked to reduced BNP levels. In individuals with a body mass index (BMI) above 30 kg/m², baseline BNP concentrations were approximately half of those observed in controls with a BMI below 25 kg/m². This phenomenon may be attributed to a higher glomerular filtration rate (GFR) in obese patients, as well as a decrease in circulating BNP, potentially due to increased binding of BNP by adipocytes [10].



Cardiac troponin serves as the primary biomarker for diagnosing acute myocardial infarction, owing to its exceptional specificity and sensitivity**.** The troponin complex, which includes troponin C, troponin I, and troponin T, is associated with tropomyosin in the cardiomyocyte's contractile apparatus. Troponin C binds to intracellular calcium, causing a conformational shift that displaces tropomyosin from the myosin-binding site, enabling myosin to interact with actin and trigger contraction in cardiomyocytes [11]. When myocardial cells are damaged, the levels of troponin I and T in the blood rise, typically peaking around 12 hours following myocardial injury. For patients suspected of having non-ST-elevation acute coronary syndrome (NSTE-ACS), elevated high-sensitivity cardiac troponin levels, either at admission or on re-testing, above the 99th percentile of healthy individuals, confirm myocardial infarction as shown in **Fig 1** [12]. Over the past decade, troponin detection assays have been optimized, including the advent of high- and ultra-sensitive troponin tests. As a result, the time needed to diagnose an acute myocardial infarction has been reduced to a maximum of 3 hours, in line with ESC and AHA guidelines. Multiple prospective studies have demonstrated that high-sensitivity troponin I levels measured 1 hour after symptom onset have a negative predictive value exceeding 99%. Troponin levels may remain persistently elevated in several chronic cardiovascular conditions, including heart failure, stable coronary artery disease (CAD), and chronic kidney disease [13]. In these patient groups, elevated troponin serves as an independent indicator of increased mortality risk and should prompt comprehensive cardiovascular follow-up. Although values exceeding the 99th percentile are traditionally used for diagnosis and prognostication, recent studies highlight the significance of even lower detectable troponin levels. Specifically, in patients presenting with acute chest pain, any measurable troponin T below the 99th percentile was associated with a twofold increase in all-cause mortality, along with heightened cardiovascular and non-cardiovascular death rates [14].

Overall, the use of biomarkers has significantly enhanced the diagnosis and prognosis of cardiovascular diseases, contributing to better patient management and outcomes.

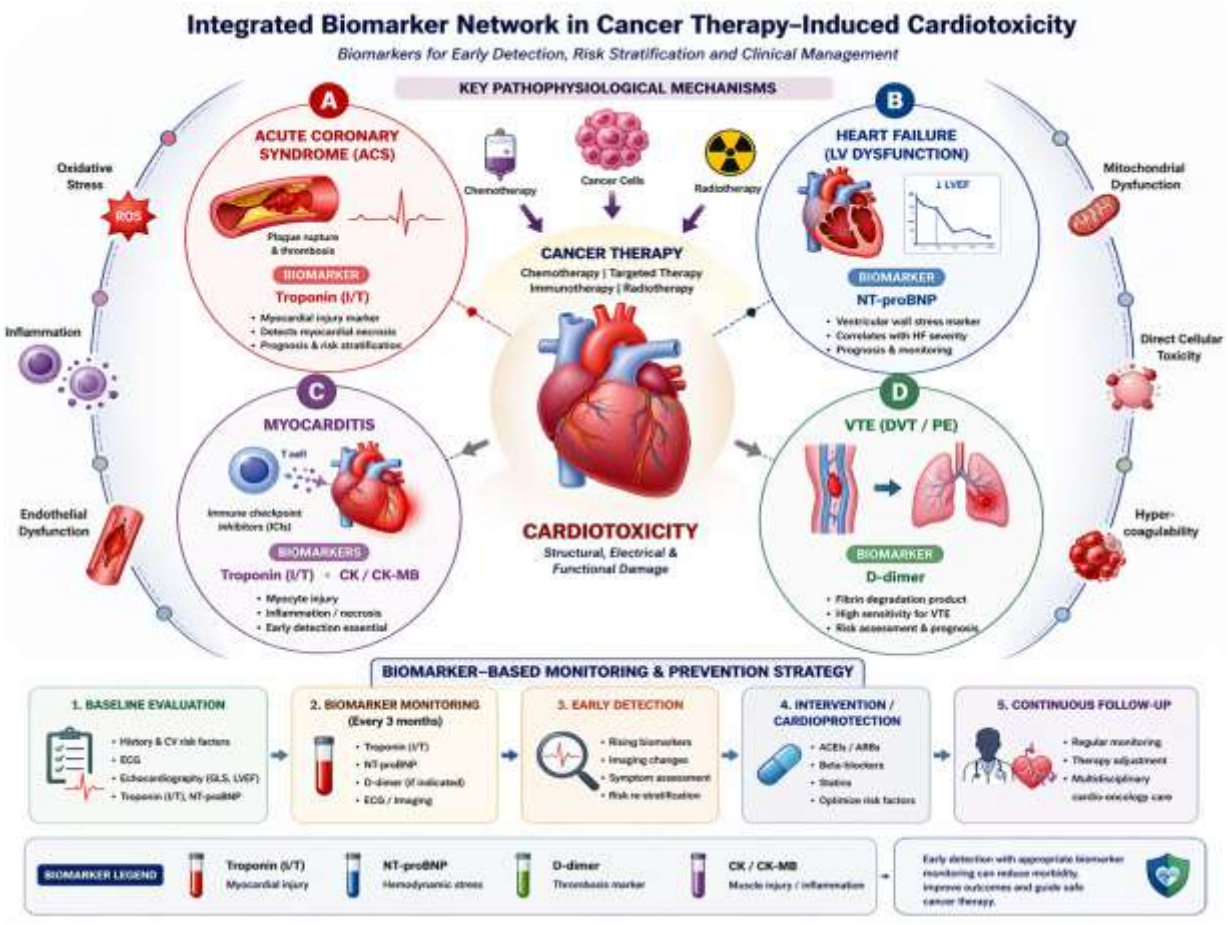


Fig.1 Integrated Biomarker Network in Cancer Therapy–Induced Cardiotoxicity

2.1 Heart failure

Both cancer and cancer treatments contribute to cardiovascular disease in cancer patients. Comorbidities such as severe infections, anemia, and thrombocytopenia can further impact patient outcomes. Heart failure is the most common type of cancer therapy-induced cardiotoxicity [15]. Left ventricular (LV) dysfunction and heart failure can result from radiotherapy, cytotoxic chemotherapy, molecularly targeted inhibitors, and antibodies that target signal transduction pathways. Anthracyclines are responsible for the majority of both subclinical and clinical LV dysfunction. The underlying mechanisms are complex [16].

On average, 18–48% of patient's exhibit signs of left ventricular (LV) dysfunction after receiving high cumulative doses of anthracycline therapy (e.g., doxorubicin 700 mg/m²). The cardiotoxic effects of anthracyclines can be further exacerbated when combined with chest/mediastinal radiation or HER-2 inhibitors (e.g., trastuzumab), which are commonly used in breast and gastric cancer treatments [17]. Risk factors for developing anthracycline-induced cardiotoxicity include cumulative dose, intravenous bolus administration, female sex, hypertension, diabetes mellitus, and pre-existing cardiovascular disease. In a prospective study involving 2,625 patients who received anthracycline-based chemotherapy, the median time from chemotherapy completion to the development of cardiotoxicity was 3.6 months, with only 11% of patients fully recovering. A matched-control study found echocardiographic cardiac abnormalities in 30% of long-term survivors of childhood acute lymphoblastic leukemia (ALL) who had received anthracycline therapy, with a median follow-up time of 13.3 years. Several studies suggest that conventional heart failure therapies, such as β-blockers and angiotensin-receptor blockers (AT1 blockers), may have both prophylactic and therapeutic effects in patients with anthracycline-induced heart failure. Early diagnosis is therefore critical [18].

Several common cancer drugs have been linked to the development of heart failure, including alkylating agents like cyclophosphamide and ifosfamide. Heart failure can occur acutely, within three weeks of therapy, in up to 28% of patients, and may be associated with high mortality (4,5,44,45). Additionally, molecularly targeted therapies can exhibit significant cardiotoxicity (46-50). For instance, the proteasome inhibitor carfilzomib, used in multiple myeloma treatment, caused LV dysfunction in 4%, hypertension in 12%, and peripheral edema in up to 25% in a dose-dependent manner [19]. The complete list of cancer drugs associated with LV dysfunction is extensive and beyond the scope of this review. Biomarkers have become essential tools for evaluating cancer therapy-induced heart failure, with troponin and BNP/NT-proBNP being the most studied biomarkers in both retrospective and prospective cardiotoxicity studies [20].

2.1.1 Natriuretic Peptides

Anthracyclines and many other cancer therapies can induce chronic heart failure. However, the relationship between serum BNP levels and chronic cardiotoxicity remains inconsistent in observational and experimental studies. A recent meta-analysis of eight independent case-control studies involving 695 anthracycline-treated patients showed a small but statistically significant correlation between the onset of anthracycline-induced cardiotoxicity and post-treatment BNP levels [21]. This correlation was more pronounced in Asian populations compared to European cohorts. In a prospective study of cancer patients, NT-proBNP was found to be a predictor of all-cause mortality. However, two other studies did not show an association between plasma NT-proBNP levels and the development of LV dysfunction or manifest heart failure [22]. Children undergoing cytotoxic cancer therapy are at high risk for developing LV dysfunction. In a randomized controlled study, 205 children with high-risk acute lymphoblastic leukemia (ALL) were either treated with doxorubicin alone or with doxorubicin plus the cardioprotective agent dexrazoxane [23]. Children treated with doxorubicin alone showed a higher frequency of elevated NT-proBNP compared to those treated with both doxorubicin and dexrazoxane. Serum troponin T was elevated in 47% of children treated with doxorubicin alone, compared to 13% in the dexrazoxane group, and was associated with a decreased LV ejection fraction (LVEF) after 90 days. In children with hematologic malignancies treated with anthracyclines, the role of angiotensin-converting enzyme inhibitors (ACE inhibitors) was explored in a double-blind, prospective trial. After six months, NT-proBNP levels in placebo-treated patients increased from a baseline of <5 ng/mL to 98.6 ng/mL. In contrast, children treated with enalapril had a 50% lower NT-proBNP level of 49.6 ng/mL, along with higher LVEF. These findings suggest that BNP plays a role in monitoring cardioprotective therapy in children receiving

anthracycline-based chemotherapy [24]. Two studies investigating plasma BNP/NT-proBNP in long-term survivors of childhood cancer, involving a total of 206 patients, found a correlation between elevated NT-proBNP levels and cumulative anthracycline dose, as well as with LV dysfunction. Overall, BNP/NT-proBNP levels have been associated with cancer therapy-related chronic heart failure in both adult and pediatric cancer patients [25].

Acute heart failure induced by cancer therapy can be a life-threatening condition. High-dose cyclophosphamide is commonly used in hematologic malignancies before bone marrow transplantation, but it can acutely cause severe heart failure with high mortality [26]. The presence of significant comorbidities in patients undergoing high-dose chemotherapy for bone marrow transplantation complicates both diagnosis and treatment. As a result, screening for cardiovascular risk factors and pre-existing conditions, along with close monitoring for cardiovascular adverse events, is essential [27]. In a small cohort of patients undergoing bone marrow transplantation, weekly BNP measurements successfully identified all patients with therapy-related heart failure (20%), though with a specificity of 43%. The authors note that comorbidities such as anemia, sepsis, fluid imbalance, or renal failure may reduce the diagnostic accuracy of BNP in these cases. In conclusion, BNP/NT-proBNP monitoring is useful for detecting acute cancer therapy-induced heart failure [28].

Troponin has been investigated as a marker for manifest heart failure in both retrospective and prospective studies. In a study involving 204 cancer patients receiving anthracycline-based or alkylating high-dose chemotherapy, elevated troponin I was linked to a significant reduction in left ventricular ejection fraction (LVEF) after seven months [29]. In contrast, patients with negative troponin I levels experienced only a transient and less significant reduction in LVEF. In a cohort of 211 high-risk breast cancer patients, a correlation between elevated troponin I and LVEF reduction (12% vs. 2%) was observed over 12 months. Troponin I levels at the end of anthracycline therapy (maximum troponin I) and three months' post-therapy were predictive of cardiotoxicity. Trastuzumab-induced heart failure, characterized by reduced LVEF, was more frequently observed in patients with elevated troponin I [30]. Data on repeated troponin measurements during cancer therapy are limited. A prospective study of 703 cancer patients undergoing high-dose chemotherapy showed that sustained troponin I elevation one month after therapy was associated with a more significant decrease in LVEF and higher rates of adverse outcomes, including cardiac death, pulmonary edema, overt heart failure, LVEF reduction >25%, and life-threatening arrhythmias, compared to isolated troponin I elevation immediately after therapy [31]. In a smaller prospective study, serial troponin I measurements in breast cancer patients revealed that a faster increase in troponin I levels during chemotherapy was associated with clinically evident heart failure or a decline in LVEF to <50% over a three-year follow-up. Recent studies indicate that combining echocardiographic evaluation with troponin measurement may improve the prediction of cardiotoxicity. Global longitudinal strain (GLS), increasingly used as a measure of myocardial function, was combined with troponin T measurement to enhance sensitivity from 86% to 93% in a small group of patients treated with the anthracycline epirubicin [32]. Either impaired GLS or elevated troponin T was associated with a 15-fold increased risk of LV dysfunction.

Troponin levels have also been shown to predict the response to heart failure therapy in cases of manifest cardiotoxicity, and studies support the benefits of biomarker-guided therapy. In a study of 251 patients receiving trastuzumab, LVEF recovery was less frequent in patients with elevated troponin I compared to those with normal troponin I levels (35% vs. 100%) [33]. The role of troponin I in guiding preventive therapy for cardiotoxicity has also been assessed in a cohort of 473 cancer patients undergoing various high-dose chemotherapy regimens. A total of 114 patients (26%) with elevated peak troponin I levels greater than 0.07 ng/mL were considered "at risk" for cardiotoxicity. These patients were randomly assigned to receive either the ACE inhibitor enalapril or no treatment for one year. In the control group, a significant and sustained decrease in left ventricular ejection fraction (LVEF) was observed, while LVEF remained stable in the enalapril-treated group [34]. However, a recent prospective trial failed to show any benefit of a troponin-guided approach compared to a troponin-independent preventive strategy using enalapril. Several recent randomized prospective studies have examined both preventive and therapeutic interventions for cancer therapy-induced LV dysfunction. The OVERCOME trial (Prevention of Left Ventricular Dysfunction with Enalapril and Carvedilol in Patients Undergoing Intensive Chemotherapy for Malignant Hemopathies) evaluated the effects of enalapril and carvedilol when administered before chemotherapy over a six-month period [35]. After six months, patients treated with enalapril and carvedilol maintained stable LVEF, whereas LVEF decreased in the control group. Additionally, control patients experienced higher rates of combined death or heart failure. High-sensitivity troponin I

and BNP levels were measured before and after chemotherapy cycles. Surprisingly, both biomarkers showed no significant differences between the intervention and control groups, and no correlation was found between LVEF and troponin I or BNP levels [35]. The PRADA trial (Prevention of Cardiac Dysfunction During Adjuvant Breast Cancer Therapy) focused on preventive treatments for cardiotoxicity in 130 breast cancer patients undergoing anthracycline-based chemotherapy, trastuzumab (22%), and radiotherapy (70%). Patients were randomly assigned to receive either candesartan, metoprolol, or a placebo. MRI-guided LVEF assessments showed a small but statistically significant improvement in LVEF in the candesartan-treated group (1.8% difference), while metoprolol had no effect. However, metoprolol did reduce the increase in troponin levels in the control group, while candesartan did not. In the CECCY trial (Carvedilol for Prevention of Chemotherapy-Related Cardiotoxicity), decreased serum troponin I levels were noted at 9 and 12 months in breast cancer patients undergoing anthracycline and cyclophosphamide therapy who were treated with carvedilol, compared to those receiving placebo. However, the study did not establish a connection between elevated troponin I levels and LVEF or heart failure symptoms [36].

2.1.2 Monitoring and prevention of therapy-induced heart failure using biomarkers

For patients scheduled to undergo cardiotoxic cancer therapies, a thorough baseline evaluation is recommended. This should include clinical examination, ECG, echocardiography with strain imaging, and measurement of cardiac biomarkers such as troponin I/T and NT-proBNP. If baseline results reveal any abnormalities—such as an ejection fraction below 50%, impaired global longitudinal strain (GLS), or elevated troponin or NT-proBNP levels it is advisable to initiate treatment with an ACE inhibitor, AT1 receptor blocker, or beta-blocker [37]. Additionally, cardiovascular risk factors should be closely monitored and managed appropriately. Lipid management, particularly dyslipidemia, is crucial. Elevated low-density lipoprotein (LDL >100 mg/dL) has been linked to a higher incidence of heart failure in breast cancer patients treated with anthracyclines [38]. Statin therapy not only reduces LDL levels but also provides anti-inflammatory and antioxidant benefits, potentially offering protection against cardiotoxicity. Therefore, early initiation of statin therapy may be beneficial. Throughout treatment, it is recommended to perform echocardiography and assess troponin and NT-proBNP levels every three months.

If elevated troponin levels are detected, especially in combination with changes in troponin levels over time, chest pain, or ECG abnormalities, acute coronary syndrome (ACS) should be suspected. In such cases, patients should be managed in accordance with ESC/AHA guidelines, including consideration of coronary angiography as shown in **Table 1** [39].

Table 1. Biomarker-Based Monitoring and Prevention Strategies for Cancer Therapy–Induced Heart Failure

S. No.	Key Aspect	Description	Reference
1	**Baseline Evaluation**	Perform clinical examination, ECG, echocardiography (with strain imaging), and measure biomarkers such as troponin and NT-proBNP before initiating cardiotoxic cancer therapy.	[30]
2	**Risk Identification**	Patients with abnormal baseline findings (LVEF <50%, impaired GLS, elevated troponin/NT-proBNP) are considered high-risk for cardiotoxicity.	[40]
3	**Preventive Pharmacotherapy**	Initiate cardioprotective drugs such as ACE inhibitors, AT1 receptor blockers, or β-blockers in high-risk patients to prevent heart failure.	[41]
4	**Management of Cardiovascular Risk Factors**	Control comorbidities like hypertension, diabetes, and dyslipidemia; statins may provide additional cardioprotective effects due to anti-inflammatory properties.	[42]

5	**Ongoing Monitoring**	(every 3 months) echocardiography and biomarker assessment (troponin, NT-proBNP) during cancer therapy for early detection of cardiotoxicity.	[43]
6	**Management of Acute Events**	Elevated troponin with symptoms (e.g., chest pain, ECG changes) suggests acute coronary syndrome; manage according to standard cardiology guidelines including possible coronary angiography.	[44]

2.2 CAD and ACS

Many cancer treatments can either trigger or worsen both acute and chronic damage to the coronary arteries. The interplay between cancer itself, cancer therapies, and pre-existing cardiovascular risk factors significantly contributes to the development of acute coronary syndrome (ACS). Malignancies often promote a chronic inflammatory state. In preclinical studies, cancer cells have been shown to release inflammatory cytokines, which damage the endothelium and accelerate the progression of atherosclerosis. Additionally, cancer frequently fosters a prothrombotic vascular environment. Common cardiovascular risk factors such as hypertension, hypercholesterolemia, smoking, and a history of coronary artery disease (CAD) further heighten the risk of ACS [45]. As cancer treatments extend life expectancy, the baseline risk of CAD in these patients also increases. Regular monitoring of blood pressure and LDL cholesterol levels is advised for cancer patients.

Radiotherapy can affect multiple cardiac structures, including coronary arteries, valves, the pericardium, and the myocardium. Patients undergoing radiotherapy face a particularly high risk of developing CAD and ACS. Radiation induces the release of inflammatory cytokines, which contribute to fibrotic and sclerotic changes in coronary vessels rather than classic atherosclerosis [46]. It also damages endothelial cells, causing them to become senescent, produce more reactive oxygen species and adhesion molecules, and reduce nitric oxide production. These processes promote atherosclerosis and myocardial fibrosis, leading to diastolic dysfunction and potentially heart failure with preserved ejection fraction (HFpEF). Therefore, both CAD and heart failure can emerge following radiation exposure [47].

Research into early detection of cardiac damage from radiotherapy using biomarkers has shown that left-sided chest radiation can increase high-sensitive troponin and CK-MB levels. However, a consistent link between radiation-induced troponin elevation and left ventricular (LV) dysfunction has yet to be established. Data on BNP's role in radiation-related cardiotoxicity is limited. Two prospective studies in breast cancer patients showed elevated BNP levels up to a year post-radiation, which correlated with radiation dose but not with clear signs of LV dysfunction or CAD [48].

Acute myocardial ischemia due to endothelial dysfunction, vasospasm, or thrombosis is a known adverse effect of fluoropyrimidines such as 5-fluorouracil (5-FU). This drug can cause endothelial injury and vasospastic reactions, resulting in clinical ischemia in up to 18% of patients—typically early during treatment. Calcium channel blockers and nitrates have shown effectiveness in treating 5-FU-induced vasospasms. Similarly, taxanes like paclitaxel and docetaxel, though less common, can cause troponin-positive vasospastic ACS [49]. Cisplatin is also known to promote arterial thrombosis in both cerebral and coronary vessels through endothelial damage and procoagulant effects, potentially resulting in ACS during treatment or hastened CAD progression. Additionally, high-dose anti-VEGF therapy with agents like bevacizumab has been associated with a 4.4-fold increased risk of cardiac and cerebral ischemic events. Tyrosine kinase inhibitors (TKIs) with anti-VEGF properties, such as regorafenib, also elevate the risk of myocardial ischemia. VEGF-targeting therapies are further linked to arterial hypertension, contributing to long-term CAD development. Collectively, these findings illustrate the diverse ways cancer therapies can contribute to ACS risk, though the exact mechanisms remain incompletely understood [50].

Diagnosing ACS in cancer patients is often complex due to atypical symptom presentation compared to non-cancer patients. Only about 30% report chest pain and 44% experience dyspnea during ACS events. Symptoms are especially less frequent in non-ST-segment elevation ACS (NSTE-ACS) versus ST-segment elevation myocardial infarction (STEMI). Reduced angina symptoms may be due to analgesics or cancer-related neuropathy [51]. Consequently, the ESC and AHA guidelines

recommend assessing cardiac biomarkers alongside ECG, symptom history, risk factors, and cancer treatment details when evaluating suspected NSTE-ACS. There is currently no specific evidence supporting the 1-hour troponin rule in cancer patients.

In suspected ACS, timely evaluation of hemoglobin, platelet count, and coagulation status is essential-especially if percutaneous coronary intervention (PCI) is planned. If myocardial infarction is confirmed, PCI should proceed as per standard guidelines. Notably, PCI outcomes in cancer patients with acute STEMI are similar to those in non-cancer patients. However, anemia (defined as hemoglobin <12 g/dL in women and <13 g/dL in men) is an independent predictor of all-cause mortality. Therefore, it is crucial to determine the most appropriate interventional approach in close coordination with the patient's oncology team [52].

2.3 Myocarditis

In the past three years, immune checkpoint inhibitors (ICIs) have become widely used in the treatment of advanced cancers. Immune checkpoints such as cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) and programmed death-1 (PD-1) normally help regulate the immune system by preventing excessive immune responses that could harm healthy cells. However, cancer cells can hijack these mechanisms to evade immune detection. ICIs work by blocking these checkpoints, thereby reactivating T-cell responses against tumor cells [53]. Since 2016, ICIs have been approved for the treatment of various malignancies, including bladder cancer, renal cell carcinoma, head and neck cancers, Hodgkin's lymphoma, and Merkel cell carcinoma.

Initial evidence for the role of immune checkpoints in preserving cardiac function came from studies in checkpoint-deficient mouse models. Mice lacking CTLA-4 or PD-1 developed fulminant heart failure, with PD-1 deficiency leading to the formation of anti-troponin I antibodies, which is believed to be the key mechanism behind the cardiac injury. Since 2016, numerous clinical case reports have documented fulminant autoimmune myocarditis associated with immune checkpoint inhibitor (ICI) therapy [54]. Recent findings estimate the prevalence of ICI-related myocarditis to be as high as 1.14%, with mortality rates ranging from 36% for monotherapy to 67% for combination therapy, typically occurring within 17 to 34 days after treatment initiation. Most affected patients present with severe heart failure, and complications such as life-threatening arrhythmias and cardiogenic shock are common, often requiring intensive care, inotropes, or extracorporeal life support [55].

Given the aggressive nature of ICI-associated myocarditis, early identification is critical for effective management. The American Society of Clinical Oncology (ASCO) recommends a structured diagnostic approach. Baseline evaluation should include ECG and troponin measurements. Because myocarditis often develops within the first six weeks of ICI therapy, weekly monitoring of ECG and troponin during the first four weeks is advisable. If symptoms develop, further assessment with ECG, echocardiography, chest X-ray, and measurements of troponin and NT-proBNP should be conducted. Elevated troponin levels have been reported in 94% of myocarditis cases, and all patients experiencing major adverse cardiac events (MACE) had elevated troponin levels [56]. In contrast, NT-proBNP showed lower sensitivity (66%) and did not correlate with MACE. Measurement of total CK, CK-MB, myoglobin, and lactate dehydrogenase is also recommended due to the frequent occurrence of concurrent peripheral myositis.

Immunosuppressive therapy with corticosteroids, alongside optimized heart failure treatment and permanent discontinuation of ICI therapy, has shown positive outcomes in retrospective studies and case reports. ASCO guidelines advise initiating high-dose corticosteroids (e.g., prednisone 1–2 mg/kg) as first-line treatment. Evidence suggests that higher initial steroid doses may be linked to lower troponin levels at discharge. Additional therapies—such as mycophenolate, infliximab, intravenous immunoglobulins, or antithymocyte globulin—have also been used successfully in isolated cases[57].

2.4 VTE

Patients undergoing cancer treatment are at an increased risk of developing deep vein thrombosis (DVT) and pulmonary embolism (PE). D-dimer, a small fibrin degradation product found in the bloodstream, is commonly used as a biomarker for thrombotic events. However, its levels can be elevated in various non-thrombotic conditions such as trauma, inflammation, and malignancy, making it unreliable for confirming venous thromboembolism (VTE) on its own.

Cancer creates a hypercoagulable state through the release of procoagulant substances and inflammatory mediators, significantly increasing the incidence of VTE compared to the general population. The risk varies depending on the cancer type and stage, and certain cancer treatments further elevate this risk [58].

Interpreting D-dimer results in cancer patients is challenging. Nevertheless, elevated D-dimer levels have been linked to poor prognosis in several types of cancer, regardless of whether VTE is present. Some studies have explored whether increasing the D-dimer threshold improves diagnostic accuracy in suspected VTE cases. Both retrospective and prospective studies identified optimal diagnostic performance at a cutoff range of 981–1,500 ng/mL, though these results haven't shown a survival benefit nor have they been externally validated [59].

In conclusion, D-dimer testing is useful for ruling out VTE in cancer patients due to its high sensitivity. However, because of its low specificity, it should not be used alone to confirm VTE. Instead, D-dimer results should be interpreted alongside other diagnostic tools, such as compression ultrasonography. Additionally, elevated D-dimer levels may indicate increased VTE risk and have been linked to the location of emboli in patients with confirmed PE.

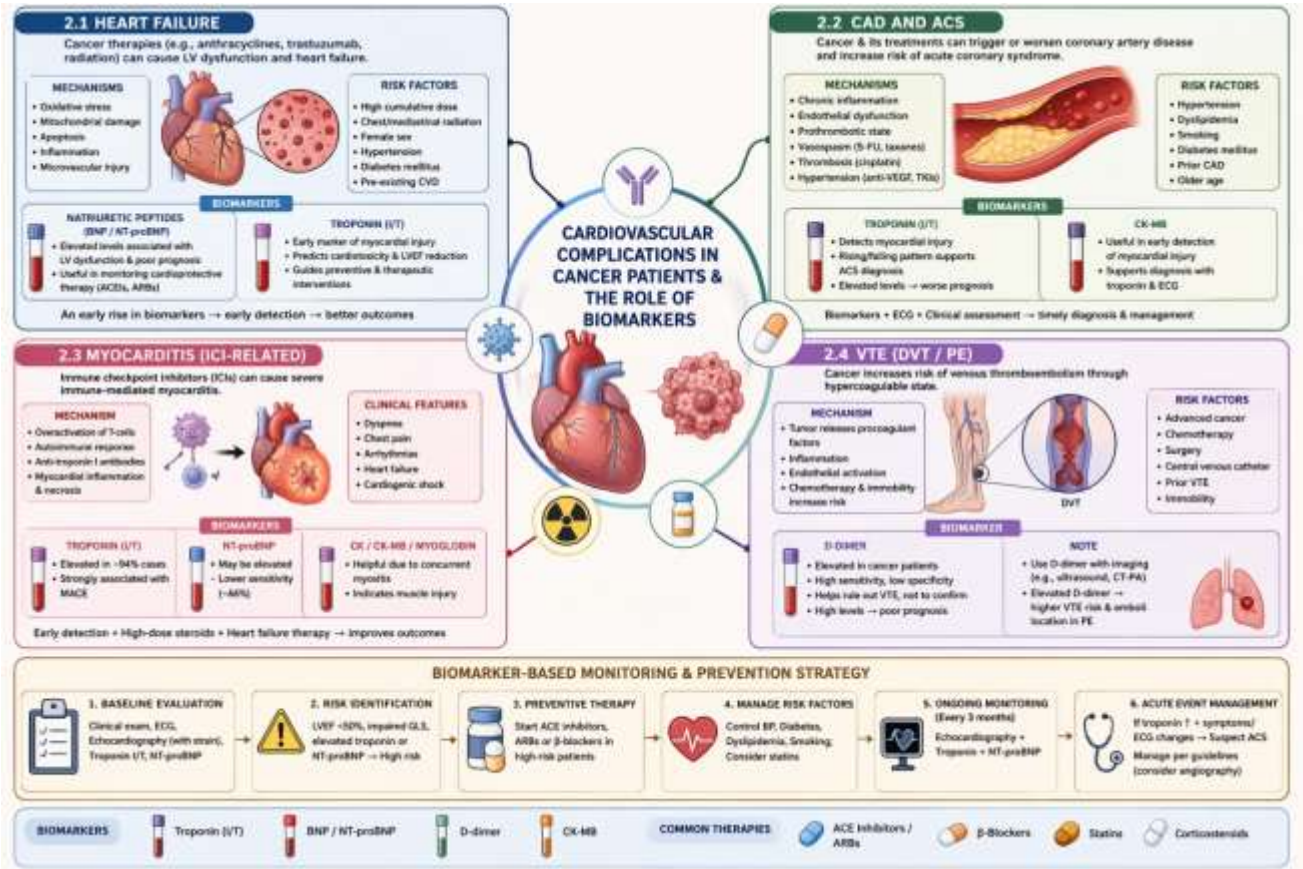


Fig.2 Cardiovascular Complications in Cancer Patients and the Role of Biomarkers

3. Future Prospective

Future research in cardio-oncology should focus on improving the early detection and prediction of cancer therapy–induced cardiotoxicity through multi-biomarker approaches, combining traditional markers (troponin, BNP/NT-proBNP) with novel biomarkers such as microRNAs and inflammatory markers. The development of personalized risk models using genomics and advanced technologies like artificial intelligence will help in better risk stratification and individualized patient care. Standardization of biomarker monitoring protocols during and after cancer therapy is also needed. Additionally, more studies are required to understand cardiovascular effects of new cancer therapies and to validate biomarker-guided preventive treatments. Strengthening cardio-oncology collaboration and focusing on long-term follow-up, especially in vulnerable populations, will be essential to improve patient outcomes.

4. Conclusion

Cancer therapy–induced cardiovascular complications represent a growing clinical challenge in the era of improved cancer survival. Biomarkers such as troponin and BNP/NT-proBNP have significantly enhanced the ability to detect, monitor, and predict cardiotoxicity, particularly heart failure, myocardial injury, and thrombotic events. However, their interpretation in cancer patients remains complex due to multiple confounding factors and variability across different therapies.

Current evidence supports the use of biomarkers as part of a multimodal approach, alongside imaging techniques and clinical assessment, for optimal risk stratification and management. Early detection through biomarker monitoring can facilitate timely intervention and potentially improve cardiovascular outcomes. Despite these advances, further large-scale studies are needed to standardize biomarker use, validate novel markers, and establish effective biomarker-guided therapeutic strategies. Strengthening collaboration between oncology and cardiology will be essential for advancing patient care. Overall, integrating biomarkers into routine clinical practice holds great promise for improving the prevention, diagnosis, and management of cardiovascular toxicity in cancer patients.

References

[1] A. A. Alshahrani, E. Kontopantelis, C. Morgan, R. Ravindrarajah, G. P. Martin, and M. A. Mamas, "Cardiovascular diseases in patients with cancer: A comprehensive review of epidemiological trends, cardiac complications, and prognostic implications," (in eng), *Chin Med J (Engl),* vol. 138, no. 2, pp. 143-154, Jan 20 2025, doi: 10.1097/cm9.0000000000003419.
[2] W. J. Hucker, Y. S. Chatzizisis, M. L. Steigner, G. L. Winters, and J. M. Kirshenbaum, "Myocardial catastrophe: a case of sudden, severe myocardial dysfunction," (in eng), *Circulation,* vol. 130, no. 10, pp. 854-62, Sep 2 2014, doi: 10.1161/circulationaha.113.007417.
[3] R. K. Upadhyay, "Emerging risk biomarkers in cardiovascular diseases and disorders," (in eng), *J Lipids,* vol. 2015, p. 971453, 2015, doi: 10.1155/2015/971453.
[4] V. Castiglione, A. Aimo, G. Vergaro, L. Saccaro, C. Passino, and M. Emdin, "Biomarkers for the diagnosis and management of heart failure," (in eng), *Heart Fail Rev,* vol. 27, no. 2, pp. 625-643, Mar 2022, doi: 10.1007/s10741-021-10105-w.
[5] R. Sarzani, M. Allevi, C. Di Pentima, P. Schiavi, F. Spannella, and F. Giulietti, "Role of Cardiac Natriuretic Peptides in Heart Structure and Function," (in eng), *Int J Mol Sci,* vol. 23, no. 22, Nov 20 2022, doi: 10.3390/ijms232214415.
[6] T. Nishikimi and Y. Nakagawa, "B-Type Natriuretic Peptide (BNP) Revisited-Is BNP Still a Biomarker for Heart Failure in the Angiotensin Receptor/Neprilysin Inhibitor Era?," (in eng), *Biology (Basel),* vol. 11, no. 7, Jul 9 2022, doi: 10.3390/biology11071034.
[7] A. Bayes-Genis *et al.*, "Practical algorithms for early diagnosis of heart failure and heart stress using NT-proBNP: A clinical consensus statement from the Heart Failure Association of the ESC," (in eng), *Eur J Heart Fail,* vol. 25, no. 11, pp. 1891-1898, Nov 2023, doi: 10.1002/ejhf.3036.
[8] M. Volpe, G. Gallo, and S. Rubattu, "Endocrine functions of the heart: from bench to bedside," (in eng), *Eur Heart J,* vol. 44, no. 8, pp. 643-655, Feb 21 2023, doi: 10.1093/eurheartj/ehac759.

[9] D. Gruson *et al.*, "The multidimensional value of natriuretic peptides in heart failure, integrating laboratory and clinical aspects," (in eng), *Crit Rev Clin Lab Sci,* vol. 61, no. 6, pp. 458-472, Sep 2024, doi: 10.1080/10408363.2024.2319578.

[10] E. N. M. Salerno *et al.*, "GLP1-RAs: long-term use versus discontinuation events of an emerging therapy for obesity and cardiovascular diseases," (in eng), *Curr Probl Cardiol,* vol. 51, no. 2, p. 103213, Feb 2026, doi: 10.1016/j.cpcardiol.2025.103213.

[11] A. M. Chaulin, "The Importance of Cardiac Troponin Metabolism in the Laboratory Diagnosis of Myocardial Infarction (Comprehensive Review)," (in eng), *Biomed Res Int,* vol. 2022, p. 6454467, 2022, doi: 10.1155/2022/6454467.

[12] A. S. Espinosa *et al.*, "Differences between cardiac troponin I vs. T according to the duration of myocardial ischaemia," (in eng), *Eur Heart J Acute Cardiovasc Care,* vol. 12, no. 6, pp. 355-363, Jun 2 2023, doi: 10.1093/ehjacc/zuad017.

[13] E. V. Geladari *et al.*, "Cardiac Troponin Levels in Patients with Chronic Kidney Disease: "Markers of High Risk or Just Noise"?," (in eng), *Diagnostics (Basel),* vol. 14, no. 20, Oct 18 2024, doi: 10.3390/diagnostics14202316.

[14] Z. Wu *et al.*, "Circulating cardiac biomarkers improve risk stratification for incident cardiovascular disease in community dwelling populations," (in eng), *EBioMedicine,* vol. 82, p. 104170, Aug 2022, doi: 10.1016/j.ebiom.2022.104170.

[15] V. Costanzo, Y. K. Ratre, E. Andretta, R. Acharya, L. Bhaskar, and H. K. Verma, "A Comprehensive Review of Cancer Drug-Induced Cardiotoxicity in Blood Cancer Patients: Current Perspectives and Therapeutic Strategies," (in eng), *Curr Treat Options Oncol,* vol. 25, no. 4, pp. 465-495, Apr 2024, doi: 10.1007/s11864-023-01175-z.

[16] C. Contaldi *et al.*, "Cancer-Therapy-Related Cardiac Dysfunction: Latest Advances in Prevention and Treatment," (in eng), *Life (Basel),* vol. 15, no. 3, Mar 15 2025, doi: 10.3390/life15030471.

[17] B. Sánchez *et al.*, "Chemotherapy-Induced Cardiotoxicity: Mechanisms, Detection and Emerging Therapies in Cardio-Oncology," (in eng), *Discoveries (Craiova),* vol. 13, no. 4, p. e217, Oct-Dec 2025, doi: 10.15190/d.2025.16.

[18] J. M. Serrano *et al.*, "Early and late onset cardiotoxicity following anthracycline-based chemotherapy in breast cancer patients: Incidence and predictors," (in eng), *Int J Cardiol,* vol. 382, pp. 52-59, Jul 1 2023, doi: 10.1016/j.ijcard.2023.04.026.

[19] A. Nagy *et al.*, "A Comprehensive Overview on Chemotherapy-Induced Cardiotoxicity: Insights into the Underlying Inflammatory and Oxidative Mechanisms," (in eng), *Cardiovasc Drugs Ther,* vol. 39, no. 5, pp. 1185-1199, Oct 2025, doi: 10.1007/s10557-024-07574-0.

[20] G. Murtagh *et al.*, "Circulating Cardiovascular Biomarkers in Cancer Therapeutics-Related Cardiotoxicity: Review of Critical Challenges, Solutions, and Future Directions," (in eng), *J Am Heart Assoc,* vol. 12, no. 21, p. e029574, Nov 7 2023, doi: 10.1161/jaha.123.029574.

[21] U. Attanasio *et al.*, "Cardiovascular Biomarkers in Cardio-Oncology: Antineoplastic Drug Cardiotoxicity and Beyond," (in eng), *Biomolecules,* vol. 14, no. 2, Feb 7 2024, doi: 10.3390/biom14020199.

[22] M. Lundgren, P. Ridefelt, M. K. Svensson, E. Hagström, T. Cars, and A. Larsson, "NT-proBNP and its correlation to left ventricular ejection fraction and heart failure - The DEMONSTRATE database," (in eng), *Ann Clin Biochem,* p. 45632251403397, Nov 17 2025, doi: 10.1177/00045632251403397.

[23] M. O. Lapointe *et al.*, "Dexrazoxane Treatments Limits Subclinical Cardiac Dysfunction in Childhood Acute Lymphoblastic Leukemia Survivors Exposed to Doxorubicin Treatments," (in eng), *J Pediatr Hematol Oncol,* vol. 45, no. 2, pp. 70-77, Mar 1 2023, doi: 10.1097/mph.0000000000002538.

[24] T. M. Alotaibi *et al.*, "Anthracyclines and the Heart: A Double-edged Sword With Therapeutic Hopes," (in eng), *J Saudi Heart Assoc,* vol. 38, no. 1, p. 2, 2026, doi: 10.37616/2212-5043.1475.

[25] S. Shyam Sunder, U. C. Sharma, and S. Pokharel, "Adverse effects of tyrosine kinase inhibitors in cancer therapy: pathophysiology, mechanisms and clinical management," (in eng), *Signal Transduct Target Ther,* vol. 8, no. 1, p. 262, Jul 7 2023, doi: 10.1038/s41392-023-01469-6.

[26] Y. Zhao, R. He, S. Oerther, W. Zhou, M. Vosough, and M. Hassan, "Cardiovascular Complications in Hematopoietic Stem Cell Transplanted Patients," (in eng), *J Pers Med,* vol. 12, no. 11, Oct 31 2022, doi: 10.3390/jpm12111797.

[27] S. K. Kunutsor and J. A. Laukkanen, "Physical activity, exercise and adverse cardiovascular outcomes in individuals with pre-existing cardiovascular disease: a narrative review," (in eng), *Expert Rev Cardiovasc Ther,* vol. 22, no. 1-3, pp. 91-101, Jan-Mar 2024, doi: 10.1080/14779072.2024.2328644.

[28] E. Haj-Yehia, L. Michel, R. I. Mincu, T. Rassaf, and M. Totzeck, "Prevention of cancer-therapy related cardiac dysfunction," (in eng), *Curr Heart Fail Rep,* vol. 22, no. 1, p. 9, Feb 19 2025, doi: 10.1007/s11897-025-00697-x.
[29] A. D'Amato *et al.*, "The Role of High-Sensitivity Troponin T Regarding Prognosis and Cardiovascular Outcome across Heart Failure Spectrum," (in eng), *J Clin Med,* vol. 13, no. 12, Jun 17 2024, doi: 10.3390/jcm13123533.
[30] A. A. Bhagat *et al.*, "Biomarkers and Strain Echocardiography for the Detection of Subclinical Cardiotoxicity in Breast Cancer Patients Receiving Anthracyclines," (in eng), *J Pers Med,* vol. 13, no. 12, Dec 14 2023, doi: 10.3390/jpm13121710.
[31] V. Sorodoc *et al.*, "The Value of Troponin as a Biomarker of Chemotherapy-Induced Cardiotoxicity," (in eng), *Life (Basel),* vol. 12, no. 8, Aug 3 2022, doi: 10.3390/life12081183.
[32] P. D. Sheth, C. Srinath, P. Mayagondanahallay Chandrashekaraiah, R. W. Madhukar, and M. Mahadevappa, ""Electrocardiographic and Echocardiographic Monitoring for Early Chemotherapy-Induced Cardiotoxicity: A Systematic Review and Meta-Analysis"," (in eng), *Echocardiography,* vol. 42, no. 11, p. e70331, Nov 2025, doi: 10.1111/echo.70331.
[33] A. Grela-Wojewoda *et al.*, "Biomarkers of Trastuzumab-Induced Cardiac Toxicity in HER2- Positive Breast Cancer Patient Population," (in eng), *Cancers (Basel),* vol. 14, no. 14, Jul 10 2022, doi: 10.3390/cancers14143353.
[34] M. S. Khan *et al.*, "Reverse Cardiac Remodeling Following Initiation of Sacubitril/Valsartan in Patients With Heart Failure With and Without Diabetes," (in eng), *JACC Heart Fail,* vol. 9, no. 2, pp. 137-145, Feb 2021, doi: 10.1016/j.jchf.2020.09.014.
[35] M. Camilli, T. Lopez-Fernandez, G. Minotti, and D. M. Cardinale, "Pharmacological strategies to prevent cancer therapy-related cardiovascular toxicity: the road to personalised cardioprotection," (in eng), *Heart,* Feb 25 2026, doi: 10.1136/heartjnl-2025-326656.
[36] M. Nabati, G. Janbabai, S. Baghyari, K. Esmaili, and J. Yazdani, "Cardioprotective Effects of Carvedilol in Inhibiting Doxorubicin-induced Cardiotoxicity," (in eng), *J Cardiovasc Pharmacol,* vol. 69, no. 5, pp. 279-285, May 2017, doi: 10.1097/fjc.0000000000000470.
[37] D. R. Lazar *et al.*, "High-Sensitivity Troponin: A Review on Characteristics, Assessment, and Clinical Implications," (in eng), *Dis Markers,* vol. 2022, p. 9713326, 2022, doi: 10.1155/2022/9713326.
[38] A. R. Tall, D. G. Thomas, A. G. Gonzalez-Cabodevilla, and I. J. Goldberg, "Addressing dyslipidemic risk beyond LDL-cholesterol," (in eng), *J Clin Invest,* vol. 132, no. 1, Jan 4 2022, doi: 10.1172/jci148559.
[39] Y. Sandoval, F. S. Apple, S. A. Mahler, R. Body, P. O. Collinson, and A. S. Jaffe, "High-Sensitivity Cardiac Troponin and the 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Guidelines for the Evaluation and Diagnosis of Acute Chest Pain," (in eng), *Circulation,* vol. 146, no. 7, pp. 569-581, Aug 16 2022, doi: 10.1161/circulationaha.122.059678.
[40] A. Greco *et al.*, "SGLT2 Inhibitors in Cancer Patients: A Comprehensive Review of Clinical, Biochemical, and Therapeutic Implications in Cardio-Oncology," (in eng), *Int J Mol Sci,* vol. 26, no. 10, May 16 2025, doi: 10.3390/ijms26104780.
[41] M. H. Strauss, A. S. Hall, and K. Narkiewicz, "The Combination of Beta-Blockers and ACE Inhibitors Across the Spectrum of Cardiovascular Diseases," (in eng), *Cardiovasc Drugs Ther,* vol. 37, no. 4, pp. 757-770, Aug 2023, doi: 10.1007/s10557-021-07248-1.
[42] R. Wasim *et al.*, "Pleiotropic Benefits of Statins in Cardiovascular Diseases," (in eng), *Drug Res (Stuttg),* vol. 72, no. 9, pp. 477-486, Nov 2022, doi: 10.1055/a-1873-1978.
[43] X. Zhang *et al.*, "Cardiac Biomarkers for the Detection and Management of Cancer Therapy-Related Cardiovascular Toxicity," (in eng), *J Cardiovasc Dev Dis,* vol. 9, no. 11, Oct 29 2022, doi: 10.3390/jcdd9110372.
[44] I. K. S. Ng, Y. W. Chia, K. C. See, and D. B. S. Teo, "Approach to acute chest pain and acute coronary syndrome in adults," (in eng), *Singapore Med J,* vol. 65, no. 2, pp. 111-118, Feb 1 2024, doi: 10.4103/singaporemedj.SMJ-2023-039.
[45] P. Kong, Z. Y. Cui, X. F. Huang, D. D. Zhang, R. J. Guo, and M. Han, "Inflammation and atherosclerosis: signaling pathways and therapeutic intervention," (in eng), *Signal Transduct Target Ther,* vol. 7, no. 1, p. 131, Apr 22 2022, doi: 10.1038/s41392-022-00955-7.

[46] T. Podlesnikar, B. Berlot, J. Dolenc, K. Goričar, and T. Marinko, "Radiotherapy-Induced Cardiotoxicity: The Role of Multimodality Cardiovascular Imaging," (in eng), *Front Cardiovasc Med,* vol. 9, p. 887705, 2022, doi: 10.3389/fcvm.2022.887705.

[47] T. Salvatore *et al.*, "Dysregulated Epicardial Adipose Tissue as a Risk Factor and Potential Therapeutic Target of Heart Failure with Preserved Ejection Fraction in Diabetes," (in eng), *Biomolecules,* vol. 12, no. 2, Jan 21 2022, doi: 10.3390/biom12020176.

[48] C. Tonry *et al.*, "Circulating biomarkers for management of cancer therapeutics-related cardiac dysfunction," (in eng), *Cardiovasc Res,* vol. 119, no. 3, pp. 710-728, May 2 2023, doi: 10.1093/cvr/cvac087.

[49] M. Rajaeinejad *et al.*, "Management of Fluoropyrimidine-Induced Cardiac Adverse Outcomes Following Cancer Treatment," (in eng), *Cardiovasc Toxicol,* vol. 24, no. 2, pp. 184-198, Feb 2024, doi: 10.1007/s12012-024-09834-9.

[50] L. Falco *et al.*, "Antioxidant Properties of Oral Antithrombotic Therapies in Atherosclerotic Disease and Atrial Fibrillation," (in eng), *Antioxidants (Basel),* vol. 12, no. 6, May 30 2023, doi: 10.3390/antiox12061185.

[51] A. Ciołek and G. Piotrowski, "Comparison of Diagnostic Parameters of Acute Coronary Syndromes in Patients with and without Cancer: A Multifactorial Analysis," (in eng), *Curr Oncol,* vol. 31, no. 8, pp. 4769-4780, Aug 20 2024, doi: 10.3390/curroncol31080357.

[52] A. Awashra *et al.*, "Reassessing PCI Timing in High Bleeding Risk Patients: Evidence, Strategies, and Outcomes," (in eng), *Catheter Cardiovasc Interv,* vol. 107, no. 3, pp. 780-794, Feb 2026, doi: 10.1002/ccd.70410.

[53] A. Naimi *et al.*, "Tumor immunotherapies by immune checkpoint inhibitors (ICIs); the pros and cons," (in eng), *Cell Commun Signal,* vol. 20, no. 1, p. 44, Apr 7 2022, doi: 10.1186/s12964-022-00854-y.

[54] S. Huang, Y. Kang, T. Liu, Y. Xiong, Z. Yang, and Q. Zhang, "The role of immune checkpoints PD-1 and CTLA-4 in cardiovascular complications leading to heart failure," (in eng), *Front Immunol,* vol. 16, p. 1561968, 2025, doi: 10.3389/fimmu.2025.1561968.

[55] L. Xu *et al.*, "A review of immune checkpoint inhibitor-associated myocarditis: Epidemiology, pathogenesis, and biomarkers," (in eng), *Hum Vaccin Immunother,* vol. 21, no. 1, p. 2512645, Dec 2025, doi: 10.1080/21645515.2025.2512645.

[56] V. K. Morris *et al.*, "Treatment of Metastatic Colorectal Cancer: ASCO Guideline," (in eng), *J Clin Oncol,* vol. 41, no. 3, pp. 678-700, Jan 20 2023, doi: 10.1200/jco.22.01690.

[57] G. Lurati Buse *et al.*, "NT-proBNP or Self-Reported Functional Capacity in Estimating Risk of Cardiovascular Events After Noncardiac Surgery," (in eng), *JAMA Netw Open,* vol. 6, no. 11, p. e2342527, Nov 1 2023, doi: 10.1001/jamanetworkopen.2023.42527.

[58] Q. Peng, J. Zhu, Y. Zhang, and Y. Jing, "Blood hypercoagulability and thrombosis mechanisms in cancer patients -A brief review," (in eng), *Heliyon,* vol. 10, no. 19, p. e38831, Oct 15 2024, doi: 10.1016/j.heliyon.2024.e38831.

[59] V. Koch *et al.*, "Cancer patients with venous thromboembolism: Diagnostic and prognostic value of elevated D-dimers," (in eng), *Eur J Clin Invest,* vol. 53, no. 4, p. e13914, Apr 2023, doi: 10.1111/eci.13914.