

Postgraduate Certificate in Cardio-Oncology (Belgium)

Pharmacological Management of Cardio-Oncology Patients

Cardiotoxicity is a central concept in cardio-oncology, describing any adverse effect of cancer therapy on the heart. It encompasses a spectrum ranging from subclinical changes in myocardial strain to overt heart failure, arrhythmias, hypertension, and pericardial disease. Understanding the mechanisms behind cardiotoxicity is essential for selecting appropriate pharmacological strategies. For example, the formation of reactive oxygen species (ROS) during anthracycline metabolism leads to mitochondrial damage, which can be mitigated by agents that scavenge free radicals.

Anthracycline-induced cardiomyopathy is one of the most studied forms of drug-related cardiac injury. Doxorubicin, epirubicin, and idarubicin are widely used in breast cancer, lymphoma, and sarcoma protocols. The risk of left ventricular dysfunction increases with cumulative dose, with a threshold of approximately 400 mg/m² for doxorubicin. Clinical practice therefore incorporates regular echocardiographic surveillance, and pharmacological prophylaxis may involve beta-blockers and angiotensin-converting enzyme inhibitors (ACEIs).

Beta-blockers such as carvedilol, bisoprolol, and nebivolol have been investigated for their cardioprotective properties. Carvedilol possesses both β -adrenergic blockade and antioxidant activity, which may reduce ROS-mediated injury. In randomized trials, carvedilol initiated before chemotherapy and continued during treatment lowered the incidence of a >10% decline in left ventricular ejection fraction (LVEF). Practical application requires titration to a target heart rate of 60–70 beats per minute, while monitoring for bradycardia and bronchospasm in patients with obstructive airway disease.

Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers (ARBs) interrupt the renin-angiotensin-aldosterone system (RAAS), a pathway that contributes to cardiac remodeling after injury. Enalapril and lisinopril have demonstrated efficacy in preventing LVEF decline when started early in the chemotherapy course. The typical dosing strategy involves initiating at a low dose (e.g., enalapril 2.5 mg daily) and up-titrating every 1–2 weeks to a target dose of 10–20 mg, provided renal function and potassium levels remain within acceptable limits. ARBs such as valsartan are alternatives for patients intolerant to ACEIs due to cough.

Statins are lipid-lowering agents that also exhibit pleiotropic effects, including anti-inflammatory and antioxidant properties. Several retrospective analyses suggest that statin therapy reduces the risk of chemotherapy-related heart failure, particularly in patients receiving anthracyclines. Atorvastatin 40 mg daily is a commonly used regimen, but clinicians must be vigilant about potential drug-drug interactions with tyrosine kinase inhibitors (TKIs) that are metabolized via the CYP3A4 pathway.

Tyrosine kinase inhibitors (TKIs) represent a class of targeted therapies that can cause a variety of cardiovascular adverse events, including hypertension, left ventricular dysfunction, and QT interval prolongation. Imatinib, sunitinib, and ponatinib are examples. The mechanism of hypertension with TKIs often involves reduced nitric oxide synthesis and increased endothelin-1 production. Management typically includes initiating an antihypertensive agent such as an ACEI or a calcium channel blocker (CCB). For instance, amlodipine 5 mg daily can be added when systolic blood pressure exceeds 140 mmHg, with careful monitoring for peripheral edema.

Calcium channel blockers are divided into dihydropyridine (e.g., amlodipine, nifedipine) and non-dihydropyridine (e.g., verapamil, diltiazem) subclasses. Dihydropyridines are preferred for TKI-induced hypertension because they have minimal impact on cardiac conduction. However, when using non-dihydropyridines in combination with certain TKIs, clinicians must consider the risk of elevated plasma concentrations due to CYP3A4 inhibition, which could increase toxicity.

QT-prolonging agents merit special attention because many oncology drugs, such as arsenic trioxide, certain FLT3 inhibitors, and some HER2-targeted therapies, can extend the QT interval and predispose patients to torsades de pointes. Baseline electrocardiography (ECG) is recommended before initiating therapy, and electrolytes (potassium, magnesium, calcium) should be corrected to maintain $K^+ > 4.0$ mmol/L, $Mg^{2+} > 2.0$ mg/dL, and $Ca^{2+} > 2.2$ mmol/L. If the corrected QT (QTc) exceeds 480 ms, dose reduction or discontinuation of the offending agent should be considered. In some cases, prophylactic use of a non-torsadogenic antiarrhythmic such as mexiletine may be explored, though evidence remains limited.

Pericardial disease can arise from radiation therapy involving the mediastinum or from immune checkpoint inhibitors (ICIs). Acute pericarditis presents with chest pain and a pericardial friction rub, while chronic constrictive pericarditis may develop months after treatment. First-line pharmacotherapy includes non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen 600 mg three times daily, with a taper based on symptom resolution. For refractory cases, colchicine 0.5 mg daily may be added, and corticosteroids are reserved for severe inflammation or when NSAIDs are contraindicated.

Immune checkpoint inhibitors (e.g., pembrolizumab, nivolumab, ipilimumab) have revolutionized cancer therapy but can trigger immune-mediated myocarditis, a potentially fatal complication. Early recognition relies on a combination of clinical suspicion, elevated cardiac troponin, and imaging findings. High-dose corticosteroids (e.g., methylprednisolone 1–2 mg/kg/day) are the mainstay of treatment, followed by a gradual taper over 4–6 weeks. In refractory myocarditis, additional immunosuppressants such as mycophenolate mofetil or infliximab may be employed, though the latter is contraindicated in patients with moderate to severe heart failure.

Myocardial strain imaging has emerged as a sensitive tool for detecting subclinical cardiotoxicity. Global longitudinal strain (GLS) values more negative than -18% are considered normal; a relative reduction of $> 15\%$ from baseline suggests early myocardial injury. Pharmacologic intervention at this stage, typically with a beta-blocker and an ACEI, has been shown to improve recovery of LVEF. Institutions often embed GLS

assessment into routine echocardiography protocols for patients receiving high-risk agents.

Biomarkers such as high-sensitivity cardiac troponin (hs-cTn) and N-terminal pro-brain natriuretic peptide (NT-proBNP) provide quantitative measures of myocardial stress or injury. Elevated hs-cTn after anthracycline infusion predicts subsequent LVEF decline, and serial measurements can guide the timing of cardioprotective medication. For example, a rise in hs-cTn above the 99th percentile may trigger initiation of enalapril 5 mg daily and carvedilol 3.125 mg twice daily, even if imaging remains unchanged.

Drug-drug interactions are a frequent challenge in cardio-oncology because patients often receive multiple agents with overlapping metabolic pathways. Many TKIs are substrates of CYP3A4, and concomitant use of strong inhibitors (e.g., ketoconazole, clarithromycin) can increase plasma concentrations, heightening the risk of cardiotoxicity. Conversely, inducers such as rifampin may reduce efficacy. A systematic medication reconciliation at each oncology visit is essential to identify and mitigate these interactions.

Renin-angiotensin-aldosterone system inhibitors not only protect against remodeling but also have a role in managing radiation-induced vascular injury. Radiation can cause endothelial dysfunction and accelerated atherosclerosis, particularly in the coronary arteries and aorta. Long-term ACEI therapy may attenuate these changes by preserving nitric oxide bioavailability and reducing inflammatory cytokine release. Clinical protocols often recommend a low-dose ACEI (e.g., ramipril 2.5 mg daily) for patients who have undergone mediastinal irradiation, with dose escalation as tolerated.

Neurohormonal antagonists such as sacubitril/valsartan combine an ARB with a neprilysin inhibitor, enhancing natriuretic peptide signaling while suppressing RAAS. Early data suggest that this combination may improve recovery of cardiac function in patients with chemotherapy-related heart failure, though robust randomized trials are pending. In practice, sacubitril/valsartan is initiated after stabilization on an ACEI or ARB, starting at 24/26 mg twice daily and uptitrating to the target dose of 97/103 mg twice daily, provided blood pressure and renal function remain stable.

Anticoagulation is frequently required in cardio-oncology due to an increased risk of venous thromboembolism (VTE) from both malignancy and certain therapies (e.g., thalidomide, lenalidomide). Direct oral anticoagulants (DOACs) such as apixaban and rivaroxaban are convenient alternatives to low-molecular-weight heparin (LMWH), but their use must be balanced against bleeding risk, especially in patients with thrombocytopenia. For patients with platelet counts between 50 000 and 100 000 μL , a reduced dose of apixaban 2.5 mg twice daily may be appropriate, while in severe thrombocytopenia (Hypertension management is a key component of care for patients receiving VEGF-targeted agents. Hypertension often appears within weeks of therapy initiation and can be severe. First-line agents include ACEIs, ARBs, or thiazide-type diuretics. In patients with pre-existing renal impairment, CCBs may be favored. Frequent blood pressure monitoring (at least weekly) during the first two months of therapy allows timely dose adjustments. If hypertension persists despite optimal medical therapy, dose reduction or temporary interruption of the oncologic agent may be necessary.

Heart failure with reduced ejection fraction (HFrEF) caused by cardiotoxic agents follows the standard guideline-directed medical therapy (GDMT) pathway, which includes a beta-blocker, an ACEI or ARB, a mineralocorticoid receptor antagonist (MRA), and, when indicated, a sodium-glucose cotransporter-2 (SGLT2) inhibitor. Empagliflozin, for instance, has been shown to reduce cardiovascular mortality and may provide additional renal protection in cancer patients who develop HFrEF. Initiation of empagliflozin 10 mg daily is safe in patients with $\text{eGFR} > 30 \text{ mL/min/1.73 m}^2$ and can be considered even during ongoing chemotherapy, provided glucose levels are monitored.

Mineralocorticoid receptor antagonists such as spironolactone and eplerenone counteract aldosterone-mediated fibrosis and sodium retention. Spironolactone 25 mg daily is commonly started after achieving stable blood pressure and renal function on ACEI/ARB therapy. Monitoring of serum potassium is mandatory, particularly when combined with potassium-sparing agents or in the setting of renal dysfunction.

SGLT2 inhibitors have entered cardio-oncology practice not only for heart failure but also for their potential renoprotective effects in patients receiving nephrotoxic chemotherapy (e.g., cisplatin). Their glucose-lowering effect can be advantageous in patients with steroid-induced hyperglycemia. However, the risk of euglycemic ketoacidosis mandates patient education on recognizing symptoms such as nausea, abdominal pain, and rapid breathing, especially during periods of fasting or acute illness.

Pharmacogenomics is increasingly relevant as genetic polymorphisms influence drug metabolism and susceptibility to cardiotoxicity. For example, variants in the NAD(P)H quinone dehydrogenase 1 (NQO1) gene can affect the detoxification of anthracyclines, while polymorphisms in the CYP3A5 gene modulate the clearance of TKIs. Incorporating pharmacogenomic testing into treatment planning allows clinicians to personalize dosing, select less cardiotoxic alternatives, and anticipate adverse events. In practice, a patient identified as a poor metabolizer of CYP3A5 may receive a reduced dose of erlotinib and be monitored more closely for QT prolongation.

Radiation-induced coronary artery disease (RICAD) develops years after mediastinal irradiation and presents as premature atherosclerosis. Prevention strategies include aggressive risk factor modification—statins, aspirin, and lifestyle counseling—combined with periodic stress testing or coronary CT angiography for high-risk individuals. When RICAD is diagnosed, revascularization decisions follow standard cardiology guidelines, but the presence of prior radiation may influence the choice between percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) due to potential tissue fibrosis.

Cardiac rehabilitation programs tailored to cancer survivors address deconditioning, fatigue, and psychological distress. Pharmacologic optimization of heart failure medications precedes enrollment, ensuring patients can safely participate in aerobic and resistance training. Exercise prescriptions typically start at 40–50 % of peak VO_2 , progressing to 70 % as tolerated, with close monitoring for arrhythmias or ischemic symptoms.

Management of arrhythmias in the cardio-oncology setting requires an understanding of the underlying etiology. Atrial fibrillation (AF) may be triggered by systemic inflammation, electrolyte shifts, or direct myocardial injury from agents such as 5-fluorouracil. Rate control is achieved with beta-blockers or non-dihydropyridine CCBs, while rhythm control may involve amiodarone, though the latter's pulmonary toxicity mandates caution in patients with prior lung irradiation. Anticoagulation decisions for AF must weigh the CHA₂DS₂-VASc score against bleeding risk, using tools such as the HAS-BLED score to guide therapy.

Amiodarone is a class III antiarrhythmic with a long half-life and extensive tissue accumulation. While effective for both ventricular and supraventricular arrhythmias, it can exacerbate radiation-induced lung injury and cause thyroid dysfunction. Baseline thyroid function tests and pulmonary imaging are advisable before initiation, and periodic monitoring thereafter is essential. In patients with significant pulmonary fibrosis, alternative agents such as dronedarone (if not contraindicated by heart failure) may be considered.

Ventricular tachycardia (VT) and ventricular fibrillation (VF) are rare but catastrophic complications of high-dose anthracyclines or certain TKIs. Immediate management follows advanced cardiac life support (ACLS) protocols, with defibrillation for VF and synchronized cardioversion for unstable VT. Long-term prevention may involve an implantable cardioverter-defibrillator (ICD) in patients with persistent LVEF. Implantable cardioverter-defibrillators and cardiac resynchronization therapy (CRT) devices require careful consideration of infection risk, especially in immunocompromised patients. Antibiotic prophylaxis and meticulous sterile technique during implantation reduce the incidence of device-related infections. In patients receiving ongoing chemotherapy that suppresses neutrophil function, device placement may be deferred until marrow recovery, unless emergent implantation is indicated.

Pharmacologic stress testing using agents such as regadenoson or adenosine is sometimes required for patients unable to exercise. However, these vasodilators can provoke bronchospasm in patients with underlying pulmonary disease, a common scenario after thoracic radiation. In such cases, dipyridamole or low-dose dobutamine may be safer alternatives, though the latter can increase heart rate and potentially precipitate arrhythmias in patients with existing conduction abnormalities.

Drug-induced pericardial effusion may accompany certain immunotherapies, particularly checkpoint inhibitors. Large effusions causing tamponade require emergent pericardiocentesis and systemic corticosteroids. Serial echocardiography is recommended for early detection, and low-dose colchicine can be used for prophylaxis in patients with prior pericarditis episodes.

Vascular toxicity associated with anti-VEGF agents can manifest as arterial hypertension, arterial thromboembolism, and endothelial dysfunction. Prophylactic low-dose aspirin (81 mg daily) is sometimes employed to reduce the risk of arterial events, but clinicians must balance this against the heightened bleeding tendency in thrombocytopenic cancer patients. Regular assessment of ankle-brachial index (ABI) may identify peripheral arterial disease early, allowing prompt intervention.

Pharmacologic management of hyperlipidemia in cardio-oncology patients often involves statins, but drug interactions with certain chemotherapeutics necessitate careful selection. For example, simvastatin is contraindicated with many TKIs due to CYP3A4 metabolism, whereas pravastatin, which undergoes minimal hepatic metabolism, may be safer. Dose adjustments and therapeutic drug monitoring should be employed when co-administered with agents that inhibit CYP3A4.

Management of diabetes mellitus is crucial because hyperglycemia can exacerbate chemotherapy-related cardiac injury. Metformin remains first-line unless contraindicated by renal insufficiency (eGFR). Drug-induced QTc prolongation management involves a stepwise approach: (1) identify and discontinue any non-essential QT-prolonging medications; (2) correct electrolyte abnormalities; (3) assess for congenital long QT syndrome; (4) consider dose reduction of the oncologic agent; and (5) implement continuous cardiac monitoring for high-risk patients. In selected cases, magnesium sulfate infusion (2 g over 1 hour) can stabilize the QT interval and prevent torsades.

Pharmacologic considerations in renal impairment are especially important because many cardio-oncology drugs are renally excreted. Dose adjustments based on creatinine clearance (CrCl) are mandatory for agents such as cisplatin, carboplatin, and certain TKIs. For example, carboplatin dosing follows the Calvert formula ($\text{dose} = \text{target AUC} \times (\text{CrCl} + 25)$), and the target AUC is reduced in patients with CrCl. Drug-induced thrombocytopenia can limit the use of antiplatelet agents and anticoagulants. When platelet counts fall below 20 000 μL , most anticoagulants are held, and platelet transfusion thresholds are individualized based on bleeding risk. In cases where antiplatelet therapy is essential (e.g., after coronary stenting), low-dose aspirin may be continued if platelet count remains above 50 000 μL , but the risk of bleeding must be discussed with the patient.

Cardiac monitoring protocols vary by drug class but generally include baseline assessment (ECG, echocardiography, biomarkers), periodic follow-up during therapy, and post-treatment surveillance. For anthracyclines, echocardiography is repeated after every cumulative dose of 100 mg/m^2 , while for HER2-targeted agents (e.g., trastuzumab), LVEF is assessed every three months. The integration of point-of-care ultrasound (POCUS) in oncology clinics enables rapid bedside evaluation of cardiac function, facilitating timely therapeutic adjustments.

Clinical decision-support tools such as the Cardio-Oncology Risk Score (CORS) synthesize patient-specific factors (age, baseline LVEF, cumulative anthracycline dose, presence of hypertension, diabetes) to estimate the likelihood of developing cardiotoxicity. A high CORS prompts pre-emptive initiation of cardioprotective agents and more frequent imaging. Incorporating these tools into electronic health records ensures that alerts are generated automatically, supporting real-time risk mitigation.

Multidisciplinary collaboration is the cornerstone of effective pharmacological management in cardio-oncology. The cardio-oncology team typically comprises a medical oncologist, a cardiologist specialized in heart failure, a pharmacist with expertise in oncology therapeutics, a radiation oncologist, and a nurse practitioner. Regular case conferences allow for coordinated medication adjustments, shared

decision-making, and patient education. For instance, when a patient develops hypertension on sunitinib, the oncologist, cardiologist, and pharmacist collaborate to select an appropriate antihypertensive, adjust the sunitinib dose, and schedule follow-up labs.

Patient education and adherence are vital components of therapy success. Patients should receive clear instructions on medication timing (e.g., taking ACEIs in the morning to avoid nocturnal hypotension), potential side effects, and the importance of reporting new symptoms such as dyspnea, palpitations, or swelling. Providing written materials, mobile app reminders, and access to a dedicated cardio-oncology hotline can improve adherence and early detection of adverse events.

Special populations present unique challenges. Elderly patients often have reduced physiological reserve, comorbidities, and polypharmacy, increasing the risk of drug-related toxicity. In such cases, lower initial doses of cardioprotective agents, slower titration, and more frequent monitoring are advisable. Conversely, pediatric oncology patients require age-adjusted dosing and long-term surveillance for late cardiac effects, as many survivors develop cardiomyopathy decades after treatment.

Pregnant patients undergoing cancer therapy pose a complex therapeutic dilemma. Certain agents, such as anthracyclines, are considered relatively safe in the second and third trimesters, while others (e.g., trastuzumab) are contraindicated due to fetal toxicity. Cardiac monitoring during pregnancy includes transthoracic echocardiography each trimester and measurement of NT-proBNP. Beta-blockers such as labetalol are preferred for hypertension, whereas ACEIs are avoided because of teratogenicity.

Future directions in pharmacological management include the development of novel cardioprotective agents targeting specific molecular pathways. For example, the antioxidant molecule probucol is under investigation for its ability to attenuate anthracycline-induced ROS formation. Additionally, ongoing trials are evaluating the use of selective mineralocorticoid receptor antagonists (e.g., finerenone) in preventing chemotherapy-related renal and cardiac injury. Integration of artificial intelligence (AI) algorithms to predict individual cardiotoxicity risk based on genomics, imaging, and clinical data promises to further personalize therapy.

Implementation of clinical pathways ensures consistency across institutions. A typical pathway for a patient scheduled to receive trastuzumab may include: (1) baseline LVEF assessment; (2) initiation of an ACEI and a beta-blocker if LVEF 10% or falls below 50%; (5) multidisciplinary review for dose modification or temporary discontinuation of trastuzumab; and (6) long-term follow-up at six-month intervals after therapy completion. Such algorithms reduce variability and improve outcomes.

Monitoring for subclinical dysfunction using strain imaging and biomarkers allows for earlier intervention. In practice, a patient receiving high-dose cyclophosphamide may have hs-cTn measured before each chemotherapy cycle. A rise in troponin from baseline 3 ng/L to 12 ng/L triggers initiation of carvedilol 3.125 mg twice daily, even if echocardiography remains unchanged. Serial GLS measurements can then confirm whether myocardial deformation improves, guiding further titration.

Adverse event reporting is an essential quality-improvement activity. Oncologists and cardiologists should document all cardiac events in the institutional pharmacovigilance system, specifying the class of agent, timing, severity, and management steps taken. Aggregated data help refine risk-mitigation strategies and inform updates to treatment guidelines.

Cost considerations influence drug selection, especially in health-care systems with limited reimbursement. Generic ACEIs and beta-blockers are cost-effective choices for cardioprotection. However, newer agents such as sacubitril/valsartan or SGLT2 inhibitors may be justified in high-risk patients if they demonstrably reduce hospitalization rates. Pharmacoeconomic analyses comparing the cost of preventive therapy versus the expense of managing heart failure provide a framework for decision-making.

Drug formulation and administration can affect tolerability. For example, oral anthracycline formulations (e.g., liposomal doxorubicin) reduce peak plasma concentrations and may lower cardiotoxic risk, but they are more expensive. Intravenous infusion over 48 hours versus rapid bolus administration also influences cardiac exposure. In cardio-oncology practice, selecting the appropriate formulation is part of the individualized treatment plan.

Drug-induced electrolyte disturbances such as hypomagnesemia are common with certain chemotherapies (e.g., cisplatin) and can precipitate arrhythmias. Routine monitoring of magnesium levels before each cycle, with supplementation of 400 mg elemental magnesium orally or intravenously as needed, mitigates this risk. Concurrent use of diuretics for heart failure further necessitates electrolyte vigilance.

Management of drug-related fatigue includes addressing underlying anemia, thyroid dysfunction, and depression. Pharmacologic treatment may involve erythropoiesis-stimulating agents for chemotherapy-induced anemia, provided the patient's hemoglobin is Use of prophylactic anti-emetics must consider cardiac safety. 5-HT₃ antagonists such as ondansetron can cause QT prolongation; therefore, alternatives like palonosetron, which has a lower propensity for QT effects, may be preferred in patients receiving QT-prolonging chemotherapy. When a 5-HT₃ antagonist is necessary, ECG monitoring before and after administration helps detect any interval changes.

Implementation of telemedicine has expanded access to cardio-oncology expertise, especially for patients in remote areas. Remote monitoring devices can transmit vital signs, weight, and rhythm data to the care team, enabling early detection of decompensation. Pharmacologic adjustments can be made promptly based on real-time information, reducing the need for in-person visits.

Drug-related pulmonary toxicity can indirectly affect cardiac management. Agents such as bleomycin and checkpoint inhibitors may cause interstitial lung disease, leading to hypoxia and increased cardiac workload. When pulmonary toxicity is identified, corticosteroids are initiated, and cardioprotective medications are reassessed to avoid compounding respiratory depression (e.g., careful use of beta-blockers in patients with reduced pulmonary reserve).

Interaction between radiotherapy and systemic therapy requires timing considerations. Sequential

administration of anthracyclines followed by mediastinal radiation increases the cumulative cardiac risk more than either modality alone. When possible, separating these treatments by several weeks reduces overlapping toxicity. Pharmacologic cardioprotection is intensified during periods of combined modality therapy, often employing a triple regimen of ACEI, beta-blocker, and statin.

Use of biomarkers for risk stratification extends beyond troponin and NT-proBNP. Emerging markers such as galectin-3 and soluble ST2 reflect myocardial fibrosis and inflammation, respectively. Elevated levels may identify patients who would benefit from early initiation of antifibrotic agents such as MRAs. Although routine clinical use is still evolving, incorporating these assays into research protocols enhances understanding of pathophysiology.

Management of drug-induced hypercoagulability is relevant for agents like cisplatin, which can increase thrombin generation. Prophylactic low-dose anticoagulation with LMWH may be considered in high-risk patients, but the decision must balance bleeding risk, especially in those with thrombocytopenia. Serial D-dimer measurements can help gauge thrombotic activity and guide therapy duration.

Drug dosing in obesity poses a challenge because many chemotherapeutic agents are dosed based on body surface area (BSA). In obese patients, using an adjusted body weight rather than actual weight can prevent overdose and subsequent cardiotoxicity. For ACEIs and beta-blockers, titration should be guided by clinical response rather than weight alone, as pharmacodynamics may differ in adipose tissue.

Use of novel anticoagulants in patients with mechanical heart valves is contraindicated; however, many cardio-oncology patients have bioprosthetic valves after valve replacement. In these individuals, DOACs such as apixaban may be appropriate, provided there is no significant renal impairment. Close collaboration with cardiac surgery and hematology is essential to determine the optimal anticoagulation strategy.

Drug-induced hyperlipidemia can result from corticosteroid therapy, leading to elevated LDL cholesterol and triglycerides. Lifestyle counseling, together with statin therapy, helps mitigate cardiovascular risk. In patients receiving mTOR inhibitors, lipid elevations are common; dose adjustment or addition of a fibrate may be necessary if triglycerides exceed 500 mg/dL.

Management of drug-related peripheral edema often involves diuretics such as furosemide. However, excessive diuresis can precipitate electrolyte abnormalities and renal dysfunction. A stepwise approach begins with low-dose loop diuretics (e.g., furosemide 20 mg daily) and, if needed, addition of a thiazide diuretic for synergistic effect. Monitoring of daily weight and urine output guides titration.

Use of anti-platelet agents in patients with thrombocytopenia requires individualized thresholds. For platelet counts between 30 000 and 50 000 μ L, low-dose aspirin (81 mg daily) may be continued if the indication is strong (e.g., recent coronary stent). If counts fall below 30 000 μ L, aspirin is usually held to avoid hemorrhagic complications.

Pharmacologic strategies for preventing radiation-induced fibrosis include the use of pentoxifylline

combined with vitamin E. This regimen has shown modest benefit in reducing late skin and subcutaneous fibrosis after chest irradiation. While not directly cardioprotective, reducing overall fibrosis can improve chest wall compliance and ease cardiac assessment.

Management of drug-induced autonomic dysfunction is relevant for agents like vincristine, which may cause neuropathy and impair autonomic regulation, leading to orthostatic hypotension.

Non-pharmacologic measures such as gradual position changes, compression stockings, and adequate hydration are first-line. Pharmacologic support with fludrocortisone (0.1 mg daily) can be considered if symptoms persist.

Use of prophylactic antibiotics in neutropenic patients receiving cardiotoxic chemotherapy must consider cardiac safety. Fluoroquinolones, for instance, can prolong QT interval; therefore, alternatives such as cefepime or meropenem are preferred when QT prolongation risk is high. The choice is guided by local resistance patterns and individual patient factors.

Drug-related liver toxicity can indirectly affect cardiac therapy, as many cardioprotective agents are metabolized hepatically. Elevations in transaminases during chemotherapy may necessitate dose reductions of statins or ACEIs, which are hepatically cleared. Regular liver function tests (LFTs) are therefore incorporated into monitoring protocols.

Implementation of dose-intensity calculations helps balance oncologic efficacy with cardiac safety. For anthracyclines, maintaining dose intensity while incorporating cardioprotective agents may involve using liposomal formulations or concurrent infusion of dexrazoxane. Dexrazoxane, an iron-chelating agent, reduces free radical formation and is approved for patients receiving cumulative doxorubicin doses > 300 mg/m². Its typical dose is 10 times the anthracycline dose, administered 30 minutes before the anthracycline infusion.

Use of dexrazoxane requires awareness of potential concerns about interference with antitumor efficacy. Current evidence suggests that dexrazoxane does not compromise overall survival in breast cancer patients, but clinicians should discuss the benefit-risk profile with the patient. Monitoring includes baseline LVEF and periodic reassessment every 2–3 months during therapy.

Management of drug-induced hyperuricemia is relevant for patients receiving high-dose cytarabine or tumor lysis syndrome prophylaxis. Allopurinol (300 mg daily) or febuxostat may be used to control uric acid levels, reducing the risk of renal complications that could limit the use of ACEIs and ARBs.

Therapeutic drug monitoring (TDM) is essential for agents with narrow therapeutic windows, such as methotrexate. Maintaining serum methotrexate levels within target ranges prevents both nephrotoxicity and cardiotoxicity. Leucovorin rescue is employed to mitigate toxicity, and renal function is closely monitored to ensure effective clearance.

Pharmacologic management of chemotherapy-induced nausea and vomiting (CINV) must consider cardiac

safety. NK1 receptor antagonists (e.g., aprepitant) are generally safe, but they can interact with CYP3A4 substrates, potentially increasing levels of certain TKIs. Dose adjustments of the TKI or selection of an alternative anti-emetic may be required.

Management of drug-induced hypertension in patients with pre-existing heart failure demands a nuanced approach. Initiating a low-dose ACEI or ARB can address both hypertension and afterload reduction, but caution is needed to avoid hypotension. In patients already on a beta-blocker, adding a CCB (e.g., amlodipine) may achieve target blood pressure without compromising cardiac output.

Use of anti-oxidant supplements such as coenzyme Q10 remains controversial. While some studies suggest a modest benefit in reducing anthracycline-related oxidative stress, the evidence is not robust enough for routine recommendation. Patients should be counseled about the lack of standardized dosing and potential interactions with chemotherapy.

Management of drug-induced hyperglycemia includes insulin therapy, oral hypoglycemics, and lifestyle modifications. In patients receiving high-dose steroids, basal-bolus insulin regimens are often required, with target fasting glucose. Pharmacologic strategies for managing cancer-related cachexia may involve appetite stimulants such as megestrol acetate, which can cause fluid retention and exacerbate heart failure. When prescribing such agents, clinicians should monitor weight, edema, and cardiac function closely, and consider concurrent diuretic therapy if needed.

Drug-related autonomic neuropathy can affect heart rate variability, leading to arrhythmic risk. Assessing heart rate variability (HRV) through Holter monitoring provides insight into autonomic function. Interventions such as aerobic exercise and beta-blocker therapy can improve HRV and reduce arrhythmia incidence.

Implementation of pharmacogenetic testing for TKIs helps identify patients at high risk for cardiotoxicity. For instance, patients with a CYP3A4*22 allele may have reduced metabolism of pazopanib, leading to higher plasma concentrations and increased hypertension risk.