Cardiovascular Risk in Cancer Patients Treated with Immune Checkpoint Inhibitors: Challenges and Future Directions

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Abstract

Cardiovascular disease is the leading cause of non-cancer related mortality and morbidity among people living with or cured from cancer. Immune checkpoint inhibitors (ICIs) are systemic anti-cancer therapies that have revolutionised the treatment of numerous cancers, even achieving durable long-term responses among patients with metastatic disease. However, the pro-inflammatory effects of ICIs have been postulated to increase the risk of atherosclerotic cardiovascular disease (ASCVD) in cancer survivorship. Standard modifiable cardiovascular risk factors can further contribute to ASCVD risk during cancer survivorship but are not routinely screened and are often untreated in patients with cancer. With the expanding use of ICIs leading to improved cancer survivorship, cardiovascular risk identification and prevention will be paramount in the care of patients with cancer. This review highlights the practical challenges associated with ASCVD prevention among the growing number of patients treated with ICIs for cancer, including balancing competing mortality risks from cancer and ASCVD, the lack of ICI-specific cardiovascular risk stratification tools, potential interactions between cardiovascular and

oncological therapies, and barriers to implementation of cardiovascular screening and prevention within existing healthcare systems.

Keywords

Immune Checkpoint Inhibitors, Coronary Artery Disease, Cardiovascular Disease, Atherosclerotic Cardiovascular Disease, Cardiovascular Risk Factors, Cardio-Oncology

Abbreviations

ASCVD – Atherosclerotic cardiovascular disease

CT – Computed tomography

CAC – Coronary artery calcium

CVD – Cardiovascular disease

CVRF – Cardiovascular risk factor

CTLA-4 - Cytotoxic T-lymphocyte-associated antigen 4

FDG - 2-[^{18}F]fluorodeoxyglucose

ICI – Immune checkpoint inhibitor

irAE – Immune-related adverse event

LAG-3 - Lymphocyte-activation gene 3

PET - Positron emission tomography

PD-L1 - Programmed death-ligand 1

Introduction

Cancer survivorship has significantly improved with the rapid development of efficacious cancer therapies. Cardiovascular disease (CVD) is the leading cause of preventable non-cancer related mortality and morbidity among childhood(1) and adult cancer survivors(2). The increased risk of CVD in cancer survivorship is likely due to both diseases sharing similar risk factors (e.g. smoking, diabetes, obesity), underlying pathophysiological pathways, and development of cancer therapy-related cardiovascular toxicity (CTR-CVT) (**Figure 1**)(3). Although heart failure has historically been the foremost CTR-CVT, there has been increasing appreciation for other toxicities such as atherosclerotic cardiovascular disease (ASCVD), arrhythmias, myocarditis, and systemic and pulmonary hypertension(3). In particular, emerging concerns for ASCVD have been raised with the growing use of immune checkpoint inhibitors (ICI) in the treatment of cancer(4). Standard modifiable cardiovascular risk factors (CVRF) can further increase the long-term risk of ASCVD but are not routinely assessed in patients treated with ICIs. This review summarises the risk of ASCVD associated with ICIs and advocates for practical research into cardiovascular risk reduction among the growing number of cancer survivors treated with these agents.

Immune Checkpoint Inhibitors

Unlike conventional cytotoxic chemotherapy and molecularly targeted therapies, ICIs elicit anti-tumour effects by harnessing host immunity to recognize and eliminate cancer cells(4). The advent of ICIs has profoundly improved the prognoses of multiple highly fatal malignancies, with complete and/or durable responses observed, even in patients with widespread metastatic cancer(4). This unique observation has been reported even years after cessation of ICI therapy, suggesting a potential legacy effect from long-lasting immune stimulation(5). Although the majority of patients with advanced cancer still succumb to their malignancy, this has raised the possibility of a long-term cure in a subset of patients who respond positively to ICIs(4).

As of December 2023, the United States Food and Drug Administration (U.S. FDA) has approved ICIs targeting three immune checkpoints: cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) inhibitors, programmed death-1 (PD-1) and its ligand (PD-L1), and lymphocyte-activation gene 3 (LAG-3), for the treatment of over 20 cancers (**Table 1**)(6). In 2019, approximately half of all patients with metastatic cancer in high income countries were reportedly eligible for treatment with ICIs(7). This number is expected to grow exponentially in the near future with over 3000 ongoing immune therapy trials in Oncology, investigating newer agents and indications across different cancer stages(8). This includes earlier prescription of ICIs for localised cancer in adjuvant and neoadjuvant settings(4,6), where long-term cancer survivorship is expected to be favourable.

Cardiovascular Immune-Related Adverse Events

ICIs demonstrate a unique side effect profile, termed immune-related adverse events (irAE), which mimic autoimmune-like reactions that can occur in any organ. Acute irAEs occur during active treatment, while chronic irAEs persist after treatment cessation and may impact up to 43% of patients(9). Cardiovascular irAEs were initially thought to be uncommon but have been increasingly recognised following the rapid uptake of ICIs in contemporary cancer treatment regimens. Acute myocarditis is the most concerning and well-recognized acute cardiovascular irAE. It often occurs within the first 6 weeks of ICI commencement and may manifest indolently with abnormal cardiac biomarkers or imaging findings through to fulminant heart failure, ventricular arrhythmias, and cardiogenic shock(10). Although associated with mortality rates approximating 50%, acute ICI-related myocarditis is rare with a reported estimated incidence of 1%(10).

Atherosclerotic Cardiovascular Disease with Immune Checkpoint Inhibitors

Growing evidence supports a long-term risk of accelerated ASCVD following ICI therapy, which could affect a larger proportion of cancer patients throughout their cancer survivorship. Chronic inflammation is a well-known risk factor for atherosclerosis and long-lasting T cell activation from ICIs, especially in those with durable anticancer response, have been postulated to accelerate ASCVD(11). Although macrophages were classically thought to have been the predominant immune cell involved in atherosclerosis, the role of T cells in plaque formation and progression has become appreciated(11). T helper 1 cells (T_h1) promote atherogenesis through secretion of inflammatory cytokines such as interferon (IFN)-γ and tumour necrosis factor

(TNF)-α(11). In contrast, regulatory T cells (T_{reg}) are atheroprotective through secretion of transforming growth factor (TGF)-β and interleukin (IL)-10(11). The roles of other T cell subtypes such as T helper 2 cells (T_h2), T helper 17 cells (T_h17), and CD8 T cells, in atherosclerosis remain unclear. Numerous pre-clinical studies have demonstrated that immune checkpoint proteins PD-1/PD-L1, CTLA-4, and LAG-3 are negative regulators of atherosclerosis(12,13). PD-1/PD-L1 knockout mice have been shown to have increased atherosclerotic burden composed of CD4 and CD8 T cells and macrophages, as well as TNF-α levels(13). Additionally, CD8 T cells within these knockout mice were found to have more cytotoxic activity compared with controls(13). Thus, inhibition of immune checkpoint pathways with ICIs could accelerate plaque formation and subsequent ASCVD. In humans, small retrospective studies have suggested associations between ICI use and increased non-calcified atherosclerotic plaque volume(14,15), inflammatory activity(16) and shift towards novel T-cell dominant compositions(17,18).

In a retrospective study of 5,864 patients, Drobni et. al. reported a notable 3-fold increase in myocardial infarction, coronary revascularisation, and stroke with ICI therapy compared to matched controls(14). A meta-analysis of 48 randomized controlled trials reported congruent results with an increased risk of myocardial infarction (odds ratio 1.51, 95% CI 1.01-2.26) and stroke (odds ratio 1.56, 95% CI 1.10-2.20) observed with ICI treatment over 6.6-32.8 month follow-up(19). These risks were determined from non-mandatory adverse event reporting and the true incidence of cardiovascular events in real-world populations could be under-reported(20).

Interactions with Other Cancer Therapies

ICIs are increasingly combined with other cancer treatment modalities such as conventional cytotoxic chemotherapy, targeted therapies, and radiotherapy(4). Although these regimens have improved antineoplastic efficacy, some of these additional treatments have been independently associated with increased ASCVD risk. Vascular endothelial growth factor (VEGF) receptor inhibitors are often combined with ICIs in the treatment of renal cell carcinoma and are associated with accelerated atherosclerosis and plaque rupture(3). When cardiovascular events were analyzed prospectively in the JAVELIN Renal 101 trial investigating ICI in combination with VEGF receptor inhibitors in the treatment of advanced renal cell carcinoma, there was a 2.1% incidence of non-fatal myocardial infarction among patients receiving ICI compared to 0.7% in the control group, over follow-up of less than one year(21). In addition, platinum chemotherapy is commonly employed with ICIs in the treatment of breast, endometrial, and colorectal cancer and have been independently reported to increase risk of coronary thrombosis(3). Left chest radiotherapy is a well-described risk factor for coronary artery disease and is used in combination with ICIs in the treatment of lymphoma, breast, and oesophageal cancer(3). Although there is limited data on the cumulative cardiotoxic effects of platinum chemotherapy and radiotherapy when used in combination with ICIs, it remains biologically plausible that these combinations could amplify ASCVD risk in cancer survivorship.

Cardiovascular Risk Reduction with Immune Checkpoint Inhibitors

Increasing clinical use of ICIs together with improvements in cancer prognosis may contribute to an increase in ASCVD incidence in cancer survivors in the coming years. ICIs are often

necessary in the treatment of cancer and hence their use should be not restricted despite their association with ASCVD. Therefore, ICI therapy could be considered conceptually as a non-modifiable CVRF among cancer patients, implicating the need to focus instead on aggressive control of modifiable CVRFs(22). This permissive cardiotoxicity approach recognises the importance of life-saving cancer therapy while also attending to ASCVD risk, achieving the best possible patient outcomes from both cancer and cardiovascular perspectives(23).

CVRFs are often prevalent among patients with cancer due to aging populations globally and both conditions sharing common bidirectional risk factors such as smoking, obesity, and diabetes(24). Accordingly, 10-year ASCVD risk scores have been shown to also predict risk of future incident cancer(25). Additionally, cancer survivors are at increased risk of developing *de novo* modifiable CVRFs such as hypertension, dyslipidaemia, and diabetes after cancer therapy(1,26). Despite this, CVRFs have been reported to be underrecognized and undertreated among cancer survivors(26), leading to increased risk of both major adverse cardiovascular events and all-cause mortality(27).

ICIs have further been associated with the development of dyslipidaemia, although associations with diabetes and hypertension remain less well defined. A meta-analysis of 48 ICI trials reported a 3.7-fold increased risk of dyslipidaemia among cancer patients treated with ICIs compared to control groups(19). In this meta-analysis, exposure to ICIs included patient groups treated with monotherapy ICIs in 41 studies, combination ICIs in five studies, combination ICI with targeted therapies in three studies, and combination ICI with VEGF inhibitors and chemotherapy in one study; control arms received conventional non-ICI cancer treatments in 38 studies and placebo in 10 studies(19). In another meta-analysis of 125 trials investigating ICI monotherapy, the incidence of hyperglycaemia and new-onset type 1 diabetes with ICI use was

1.2% and 0.4% respectively over short-term follow-up (1-3 years), although no comparisons with placebo cohorts were made(28). Another meta-analysis of adverse event reporting in 32 ICI trials did not demonstrate an increased rate of newly reported hypertension, defined as blood pressure >120/80mmHg, after commencing ICIs among treatment groups when compared to control arms over median follow-up of 36 months(29). In this analysis, seven studies compared treatment groups using combination ICIs with control arms employing ICI monotherapy, whilst the remainder 25 studies compared ICI monotherapy with other non-ICI cancer therapies(29). There was no difference in rates of newly reported hypertension among those treated with dual or single ICI therapy. A retrospective analysis of 259 patients similarly reported no significant changes in systolic blood pressure after two years of ICI therapy (132mmHg at baseline vs 133mmHg at follow-up)(30). However, patients treated with combination ICIs were found to have a statistically significant 5.5 mmHg increase in systolic blood pressure from baseline (128mmHg to 134mmHg), whilst no changes were observed among those treated with ICI monotherapy(30). Although observational, these results suggest a potential for more significant hypertension with combination ICIs despite similar rates of hypertension diagnoses with ICI monotherapy.

Accordingly, both cardiovascular and oncological guidelines have recommended surveillance and treatment of CVRFs for all patients living with or treated for cancer, irrespective of cancer type or therapy(3,31,32). Despite this, several challenges hamper the application of routine cardiovascular risk reduction among patients treated with ICIs (**Figure 2**), largely due to the lack of long-term preventive cardiology data in cancer populations and understandable concerns surrounding competing cancer survival risks among patients and oncology healthcare providers. Specifically, these challenges include difficulties in patient selection for CVRF screening and

treatment, the lack of ICI-specific ASCVD risk stratification tools, interactions between cardiovascular and oncological therapies, and implementation of cardiovascular preventive care among cancer patients within existing health systems (**Graphical Abstract**).

Challenges and Future Directions

Patient Selection for Cardiovascular Risk Reduction

The 2022 European Society of Cardiology Cardio-Oncology Guidelines recommend screening and treatment of CVRFs in all patients with cancer(3). Although idealistic, this recommendation may not be practical in real-world practice due to competing oncological priorities. Despite advances in contemporary ICI regimens, the majority of cancer patients treated with these agents still suffer cancer related mortality and may not benefit from long term cardiovascular risk reduction(4). Thus, universal CVRF screening with a view to initiating cardiovascular preventive therapies could be perceived as futile (or distracting) by oncology patients and healthcare providers, affecting uptake of these recommendations(33). The addition of cardiovascular risk counselling, screening, and treatments could further add to time toxicity, defined as time spent attending healthcare visits(34), among cancer patients who often already have a high burden of appointments for cancer care. CVRF screening and treatment may also overwhelm patients with information and complicate shared decision-making processes(33). Furthermore, universal CVRF screening and treatment among cancer patients would lead to additional healthcare costs that may not be cost-effective in the setting of competing cancer risks.

Prospective registries, such as the Global Cardio-Oncology Registry (G-COR)(35), will be crucial in identifying subgroups of patients treated with ICIs that are more likely to benefit from

long-term cardiovascular risk reduction. Cost-effectiveness analyses are also required to determine ideal populations to target CVRF screening and treatment. In the meantime, deliberation should be taken to select suitable patients treated with ICIs that would benefit from CVRF screening and treatment in real-world practice. A practical approach could include conducting CVRF screening in patients expected to have favourable prognoses, such as those with localised cancer receiving curative intent (neo)adjuvant ICI or advanced disease who have achieved durable response after 1-2 years of ICI therapy (**Figure 3**). This would shift the balance of competing ASCVD-cancer risks towards greater benefit for cardiovascular risk reduction. Among patients with curative disease, CVRF screening could be introduced a period after ICI commencement when patients have become more accustomed to treatment to avoid information overload(33). Decisions surrounding preventive pharmacotherapies should be patient-centred and involve shared input from patients and treating oncologists to determine likelihood of net benefit.

Risk Stratification and Imaging Biomarkers

Cardiovascular risk is poorly defined and represented in ICI trials, with most failing to report baseline CVRFs within their recruited cohorts. In a systematic review of 69 trials that led to U.S. FDA approval of ICIs in the treatment of various cancers, only one trial recorded baseline prevalence of hypertension, dyslipidaemia, and diabetes(36). Patients with pre-existing heart failure or ASCVD have also been excluded in up to 30% of ICI trials, potentially introducing a selection bias towards cohorts with lower cardiovascular risk compared to real-world populations(36,37). Additionally, current cardiovascular risk prediction scores fail to account history of cancer and ICIs as additional risk factors for ASCVD. This has led to uncertainty

surrounding the validity and applicability of conventional ASCVD risk scores to cancer populations, particularly those treated with ICIs. The paucity of prospective data on cardiovascular risk and outcomes among patients treated with ICIs further complicates the development of ICI-specific risk stratification tools in this population.

Imaging biomarkers from routine cancer imaging have been proposed as an opportunistic tool to improve ASCVD risk stratification among patients with cancer. These include coronary artery calcium (CAC) and aortic plaque progression on cancer staging computed tomography (CT) scans (**Figure 4**), as well as aortic plaque activity on 2-[^{18}F]fluorodeoxyglucose (FDG) positron emission tomography (PET) scans. CAC and aortic plaque progression can be reliably estimated from non-gated cancer CTs and can provide additional insight into future risk of ASCVD events(14,38). FDG-PET cancer staging scans could be used to determine metabolic activity within aortic plaque as a surrogate marker for ASCVD risk following ICI commencement(16).

To develop ASCVD risk stratification tools specific to patients with cancer treated with ICIs, future ICI trials must consider prospectively recording and screening for standard modifiable CVRFs. Registry data will play an important role in determining the incidence, timing, and predictors of ASCVD after ICI treatment. Although imaging biomarkers seem promising, further research into the predictive utility, validity, implementation (including the development of semi-automated methods for measurement), and treatment strategies following high risk results are required for these parameters to be adopted into practice for ASCVD risk prediction. Subsequently, ICI-specific proformas incorporating imaging biomarkers for cardiac risk assessment and stratification can be developed similar to existing Heart Failure Association/International Cardio-Oncology Society cardiovascular risk scoring tools employed with other systemic anti-cancer therapies(39).

Interactions between Cardiovascular and Oncological Therapies

As patients with cancer are often excluded from cardiovascular trials, there is a lack of data surrounding the efficacy, safety, and potential interactions between conventional cardiovascular preventive therapies and ICIs. Statins have been associated with slower rates of aortic plaque progression in a small retrospective study of 40 melanoma patients treated with ICIs(14), however its use in preventing clinical ASCVD in larger populations and the setting of competing cancer survival risks has yet to be prospectively evaluated. From a safety perspective, there has been suggestion that statins may increase risk of skeletal myopathy when used in conjunction with ICIs, although the reported incidence was low (1.2%)(40). Data remains limited surrounding the use of other lipid-lowering agents, antihypertensives, and cardiometabolic agents within cancer populations treated with ICIs.

There is growing interest in the possibility of cardiovascular preventive therapies having synergistic anticancer effects when used concurrently with ICIs. Statins have been reported to inhibit protein prenylation and enhance tumour antigen presentation, potentially improving anti-tumour efficacy with ICIs(41). This has been reported in several small studies of patients with non-small cell lung cancer and mesothelioma, which showed improved objective response rate, progression-free survival, and overall survival with concurrent statin use during ICI treatment(42,43). Additionally, pre-clinical studies have suggested potential for proprotein convertase subtilisin/kexin type 9 inhibitors(44) and bempedoic acid(45) to synergistically enhance tumour response to ICIs. In a retrospective study of 5910 cancer patients with hypertension treated with ICIs, prescription of renin-angiotensin-aldosterone inhibitors was observed to be associated with better overall survival(46). However, further research into the

synergistic effects of these cardiovascular preventive agents with ICIs in humans are needed before definitive conclusions may be drawn.

With the increasing need for cardiovascular risk reduction in patients treated with ICIs, further data on the use of preventive pharmacotherapies for modifiable CVRFs in the setting of ICI use is desperately required. This could be obtained through more granular reporting of cardiovascular preventive therapy use within ICI trials and ongoing dedicated cardio-oncology registries. In addition to assessments for efficacy, safety, and interactions, research into appropriate treatment targets that are specific to ICI-treated populations for each standard modifiable CVRF should be considered. Further assessment of potential dual cardiovascular and oncological benefits of cardiovascular preventive therapies are also warranted with studies designed to address both cancer and cardiovascular outcomes.

Implementation of Cardiovascular Risk Reduction

As described, CVRFs remain underdiagnosed and undertreated among cancer survivors in real-world practice(26) despite recommendations from oncological and cardiovascular guidelines(3,31,32). A retrospective study of 333 patients admitted to a cardiology unit reported that patients with history of cancer, including those in remission, had lower uptake of cardioprotective medications despite having similar CVRF profiles to those without cancer(47). Similarly from a secondary prevention perspective, a registry of 35,249 patients with acute coronary syndrome reported that patients with history of cancer were less likely to be prescribed $P2Y_{12}$ inhibitors and statins compared to a matched cohort without cancer, leading to increased in-hospital cardiac mortality(48). The observed lack of implementation of guideline

recommendations for cardiovascular risk reduction highlights biases within existing health systems, which are not designed to holistically and simultaneously address both oncological and cardiovascular aspects of care required by cancer patients. Primary care physicians, oncologists, and cardiologists often practise in siloes within health systems leading to fragmentation of care. This leads to ambiguity and lack of ownership surrounding the management of CVRFs in patients with cancer(33). As oncologists are pre-occupied with cancer surveillance and treatment, the responsibility of CVRF management is commonly deferred to primary care physicians. However, primary care physicians may not be aware of heightened cardiovascular risks associated with cancer and ICI therapy or oncological and cardiovascular guideline recommendations for CVRF screening. Concerns surrounding competing cancer survival risks could also influence underutilisation of cardiovascular preventive therapies among primary care physicians. Additionally, this would lead to reduced consultation with cardiology services for management of CVRFs in patients treated with ICIs, which would further perpetuate the underdiagnosis and undertreatment of CVRFs.

To improve implementation, healthcare pathways should be designed within existing systems to allow for routine CVRF screening and protocolised downstream cardiovascular assessment and risk reduction in eligible patients. These would need to be developed primarily for primary care physicians and oncologists, who are the clinicians involved as the first point of medical contact in the journey of cancer care, and can be integrated into existing dedicated oncology rehabilitation programs. CVRF screening could be opportunistically incorporated as part of routine cancer care for patients suitable for cardiovascular risk reduction. Non-fasting lipid studies and glycosylated haemoglobin A1c can be added to pathology tests routinely performed during cancer care(49). Multiple blood pressure measurements are regularly obtained during

cancer care visits and could be repurposed into hypertension screening programs(50). The assessment of these results could be delegated to cancer nurse specialists within oncology rehabilitation programs or other existing nursing-led models of cancer care, with referrals to cardiology for cardiovascular risk reduction when required. Oncology rehabilitation programs provide an excellent avenue to promote lifestyle modification and provide exercise prescription. The development and involvement of cardio-oncology services would provide an avenue for cardiovascular risk reduction among patients treated with ICIs, removing the uncertainty surrounding clinical responsibility for CVRF management in these patients. Cardio-oncology services may also be better equipped in balancing competing risks of cancer and ASCVD and can coordinate case discussions during multidisciplinary meetings, thus improving prescription of preventive therapies in patients who stand to benefit from long-term cardiovascular risk reduction.

Patient advocate engagement will be paramount in determining the feasibility and acceptability of cardiovascular risk reduction policies within the cancer care continuum. Collaborative interaction with patient advocates can provide valuable insight into patient needs and perceptions, ensuring that appropriate models of care are developed. As a large proportion of cancer patients may be unaware of their heightened cardiovascular risks(33), patient advocates can also assist with cardiovascular health promotion to improve patient engagement with cardio-oncology services for cardiovascular risk reduction.

Conclusion

ICIs have improved the prognosis of numerous cancers with durable responses observed even in a subset of patients with advanced disease. The pro-inflammatory effects of ICIs have raised the plausibility of increased ASCVD in cancer survivorship and suggests the need for cardiovascular risk reduction in this population. The lack of preventive cardiology data in ICI-treated populations and competing survival risks from cancer complicate patient selection for cardiovascular risk reduction, cardiovascular risk assessment, and implementation of CVRF screening and treatment among patients treated with ICIs. Further prospective research and registry data are required to address these challenges and improve cardiovascular outcomes among a growing population of ICI-treated cancer survivors.

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Tables

Table 1: United States Food and Drug Administration approved indications for immune checkpoint inhibitors as of December 2023(6)

Organ	Cancer
Skin	Melanoma*
	Cutaneous squamous cell carcinoma
	Basal cell carcinoma
	Merkel cell carcinoma
Lung	Non-small cell lung cancer*
	Small cell lung cancer
	Pleural mesothelioma
Urothelial	Renal cell cancer*
	Urothelial carcinoma*

Head and neck	Squamous cell carcinoma
	Alveolar soft palate sarcoma
Gastrointestinal	Hepatocellular carcinoma
	MSI-H or dMMR colorectal cancer
	Gastric cancer*
	Oesophageal cancer*
	Biliary tract cancer
Breast	Triple negative breast cancer*
Lymphoma	Classical Hodgkin's lymphoma
	Mediastinal B cell lymphoma
Gynecological	Cervical cancer
	Endometrial carcinoma
Others	MSI-H, dMMR or TMB-H solid organ tumours

All indications are approved for advanced or metastatic settings.

*Also approved for adjuvant or neoadjuvant use

dMMR – mismatch-repair-deficient, MSI-H – microsatellite instability-high, TMB-H – tumour mutational burden-high

Figures

Graphical Abstract: Cardiovascular Risk in Patients Treated with Immune Checkpoint Inhibitors

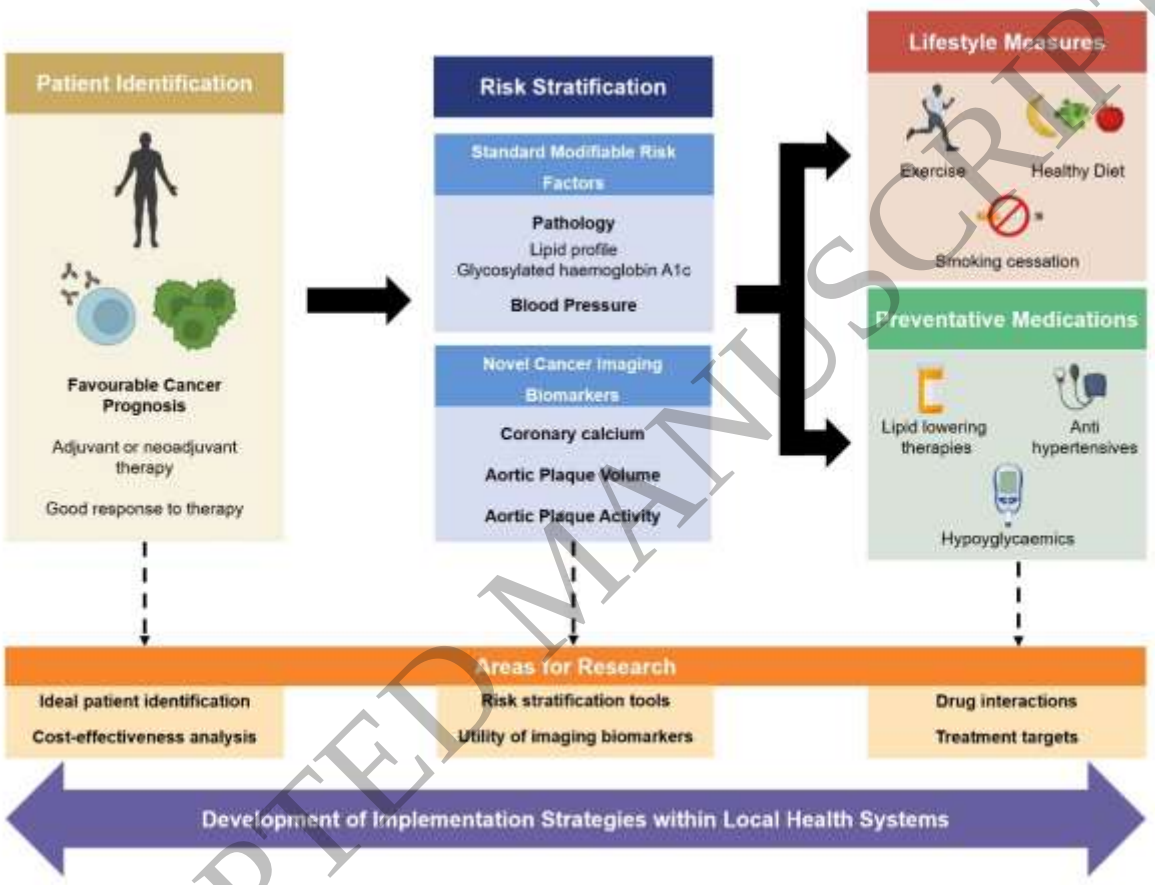
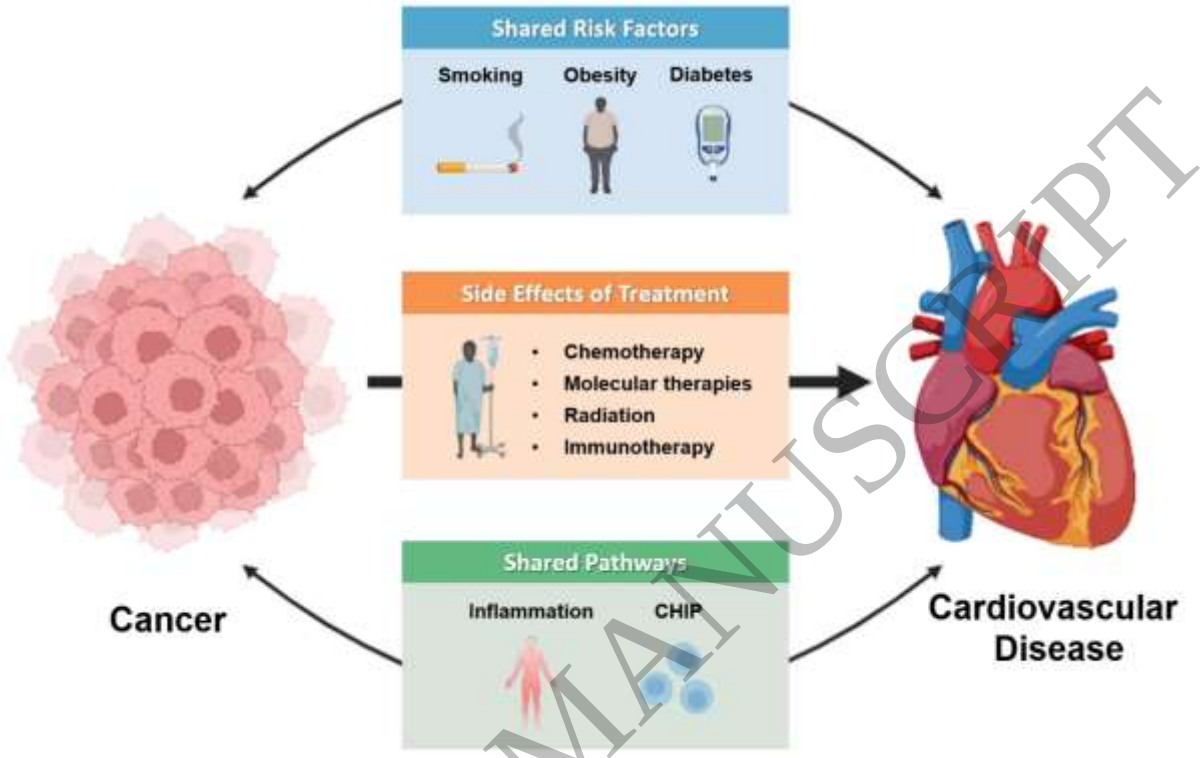


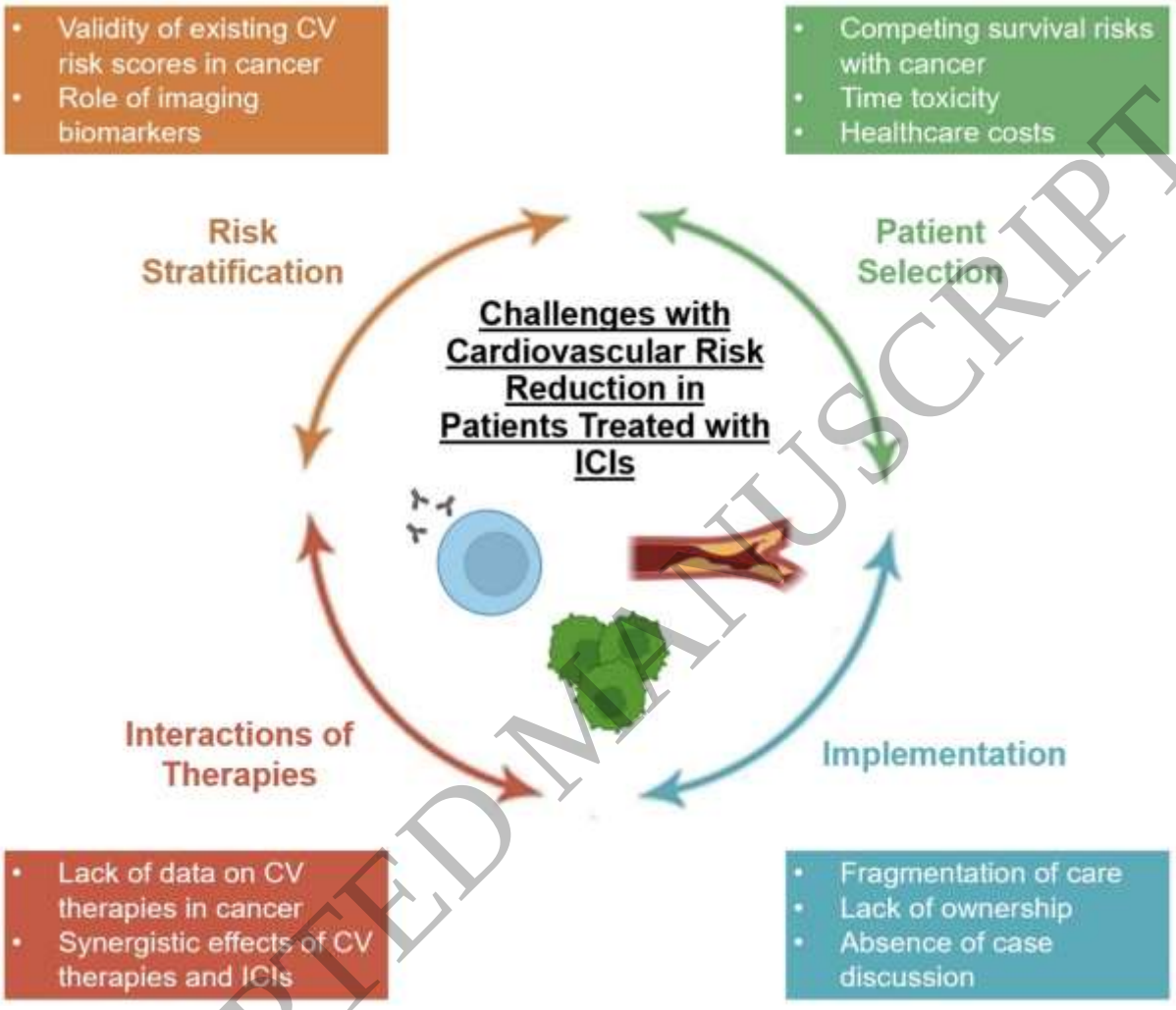
Figure 1: The association between cancer and cardiovascular disease



Cardiovascular disease and cancer have been thought to be different clinical manifestations of shared risk factors, including smoking, obesity, and diabetes, and underlying pathophysiological pathways, such as chronic inflammatory states and clonal haematopoiesis of indeterminate potential(3). Certain systemic cancer therapies have also been demonstrated to accelerate the development of cardiovascular disease.

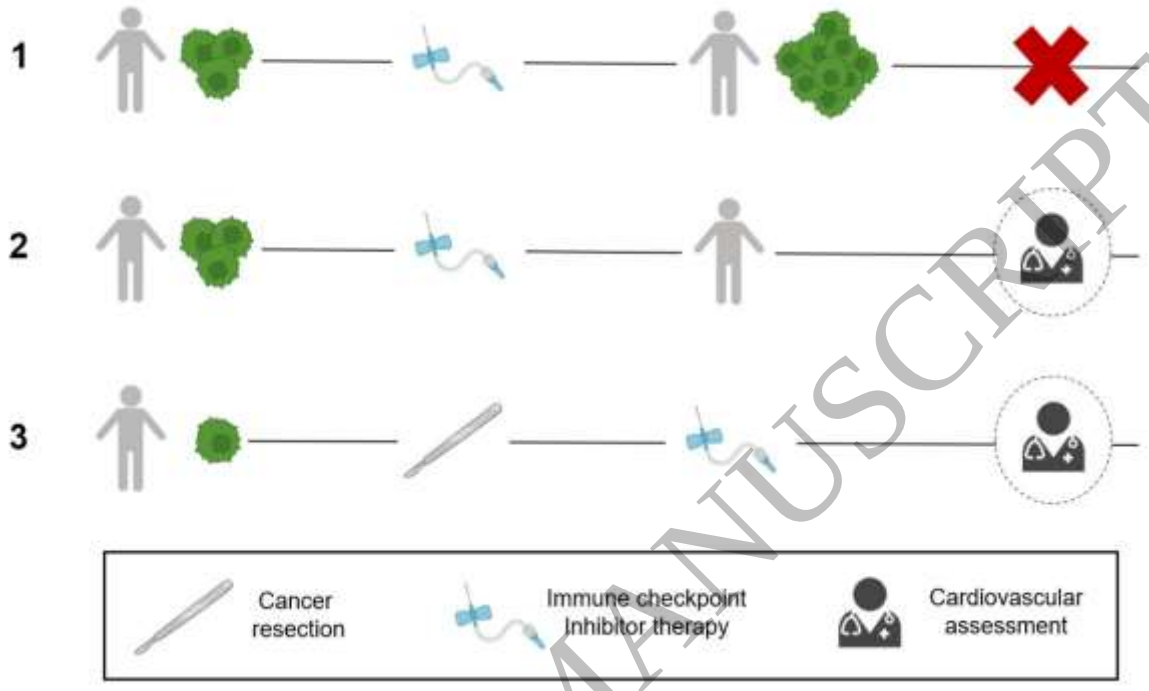
CHIP – Clonal haematopoiesis of indeterminate potential

Figure 2: Challenges with cardiovascular risk reduction



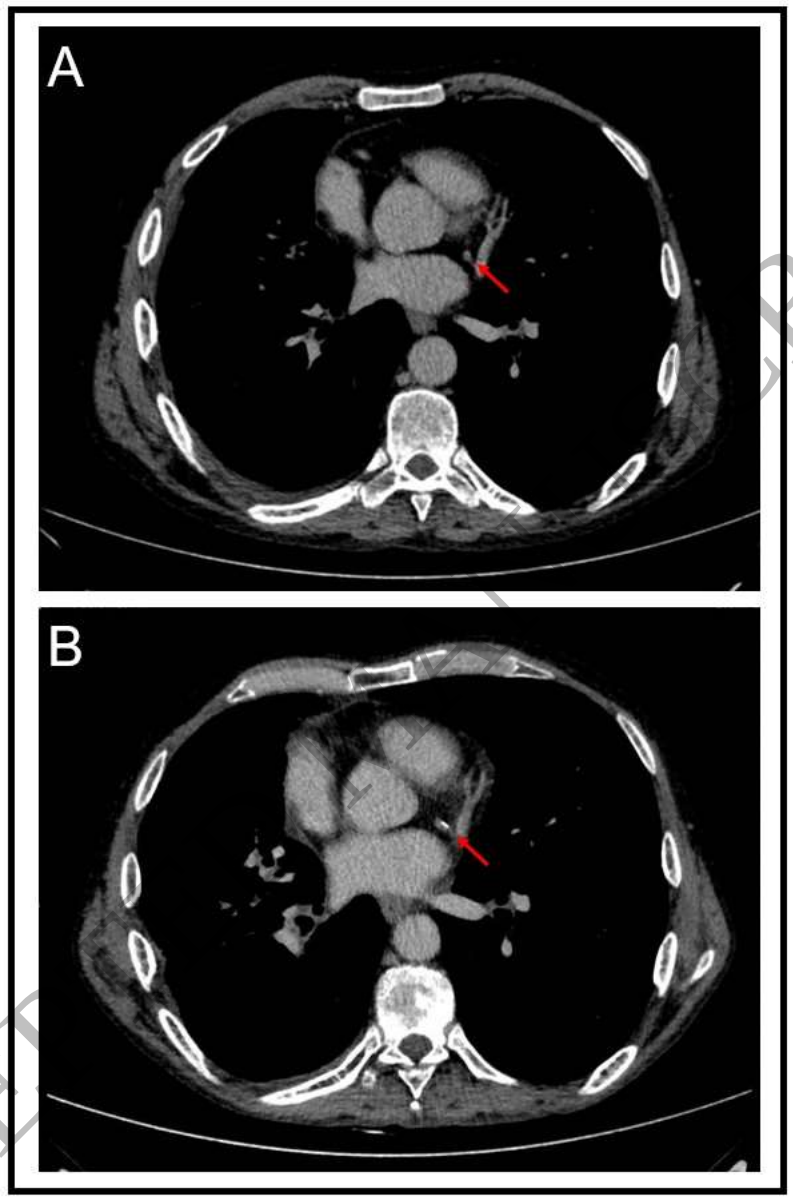
CV – cardiovascular, ICI – Immune checkpoint inhibitor

Figure 3: Patient selection for cardiovascular screening



Patients with advanced cancer who do not respond favourably to immune checkpoint inhibitor therapy should not be considered for cardiovascular risk assessment (1). Patients who may be suitable for cardiovascular risk assessment and reduction include (2) those with advanced disease who achieve durable and/or complete response and (3) those with localised cancer receiving curative intent (neo)adjuvant immune checkpoint inhibitor therapy.

Figure 4: Coronary artery calcification on non-gated cancer imaging



Red arrows demonstrate interval development of coronary artery calcification in the left circumflex artery on serial non-gated cancer staging computed tomography scans in a 47-year-old man treated with adjuvant atezolizumab for non-small cell lung cancer.