Received: 15 October 2025 | Revised: 3 March 2026 | Accepted: 21 March 2026

DOI: 10.1111/bph.70461

THEMED ISSUE REVIEW

A comprehensive review of cancer-induced cardiac wasting

Alessia Lena[1,2,3] | Muhammad Shahzeb Khan[4] | Ulrich Keller[5,6,7,8] | Lars Bullinger[5,6,7,8] | Dominik P. Modest[5,7,8] | Markus S. Anker[1,2,3,9]

[1]Department of Cardiology CBF, Angiology and Intensive Care Medicine, Deutsches Herzzentrum der Charité, Berlin, Germany

[2]Freie Universität Berlin and Humboldt-Universität zu Berlin, Charité–Universitätsmedizin Berlin, Berlin, Germany

[3]DZHK (German Centre for Cardiovascular Research), Partner Site Berlin, Berlin, Germany

[4]BSW Heart Hospital Plano, Baylor Scott and White Research Institute, Dallas and Plano, Texas, USA

[5]Freie Universität Berlin and Humboldt-Universität zu Berlin, Department of Hematology, Oncology and Tumor Immunology, Charité—Universitätsmedizin Berlin, Berlin, Germany

[6]Max Delbrück Center, Berlin, Germany

[7]German Cancer Consortium (Deutsches Konsortium Für Translationale Krebsforschung, DKTK), Partner Site Berlin, Berlin, Germany

[8]National Center for Tumor Diseases (NCT), Partner Site, Berlin, Germany

[9]School of Cardiovascular and Metabolic Health, University of Glasgow, Glasgow, UK

Correspondence
Markus S. Anker, Department of Cardiology CBF, Angiology and Intensive Care Medicine, Deutsches Herzzentrum der Charité, Berlin, Germany.
Email: markus.anker@dhzc-charite.de

Cancer is frequently accompanied by cachexia, a systemic syndrome characterized by progressive loss of skeletal muscle mass, with or without loss of fat mass. Increasing evidence indicates that cancer can also induce cardiac muscle wasting, which is associated with structural cardiac remodelling, impaired contractile function and the development of cancer-related cardiomyopathy. This cardiac involvement likely contributes to exercise intolerance, reduced quality of life and increased mortality, suggesting its prognostic significance and its potential impact as a therapeutic area within interdisciplinary cancer care. Cancer-induced cardiac wasting is driven by a complex interplay of tumour-derived and host-related factors. Although it shares some pathophysiological features with systemic cachexia, recent studies reveal that its underlying mechanisms are distinct. These mechanistic differences suggest that malignancy-associated cardiac wasting should be recognized as an independent pathological entity, which warrants dedicated diagnostic and therapeutic approaches. The aim of this review is to provide a comprehensive overview of malignant cardiac wasting in cancer, integrating evidence from preclinical models and clinical observations. We delineate the principal pathophysiological mechanisms implicated in the development of malignant cardiac wasting and critically appraise the diagnostic modalities currently employed to detect this condition in patients with cancer. Furthermore, we examine emerging preventive and therapeutic strategies aimed at preserving cardiac mass and function, ultimately seeking to improve prognosis, exercise tolerance and quality of life in affected individuals. By leveraging mechanistic, translational and clinical insights this review underscores the need for integrated cardio-oncology approaches to address this underrecognized yet clinically significant complication of cancer.

KEYWORDS
cachexia, cancer, cancer-induced cardiomyopathy, cardiac wasting

1 | INTRODUCTION

Cardiac muscle wasting is an increasingly recognized phenomenon in patients with cancer. This progressive loss of heart muscle mass and functional impairments significantly reduces quality of life and survival,

Abbreviations: MuRF1, muscle RING-finger protein; UPS, ubiquitin–proteasome system.

increasing mortality risk from cardiac dysfunction by up to 30% in some cancer types (Anker et al., 2023; Sturgeon et al., 2019; Tichy & Parry, 2023). Although systemic cachexia is the main risk factor in the development of malignant cardiac wasting, the underlying cardiac mechanisms differ from the pathogenesis of cancer cachexia. Malignant cardiac wasting is also different from other aetiologies like heart failure because it is influenced by cancer-dependent factors, including tumour biology, tumour-derived inflammation and side effects of cancer therapies such as chemotherapy and radiation therapy (Anker, Rashid, Butler, & Khan, 2025; Ausoni et al., 2020; Lena et al., 2018).

Recent advancements in therapies including supportive medicine have markedly improved the life expectancy of patients with several cancers. This positive trend in cancer survival has, nonetheless, brought a growing concern to light - many survivors develop cardiovascular complications. For example, in a cohort of 91,407 cancer survivors, risk of heart failure or cardiomyopathy was elevated (hazard ratio [HR]: 1.08; 95% confidence interval [CI]: 1.02–1.15) compared with population controls (Mulder et al., 2025). Although often attributed to the cardiotoxic effects of cancer therapies, the contribution of cancer-related cardiac wasting as a potential driver of cardiac dysfunction and heart failure is more difficult to estimate, as its mechanism and quantification are more complex than a direct drug-related organ damage. However, this potentially frequently occurring and yet underrecognized condition may compromise cardiac function and negatively impact patient outcomes. Therefore, understanding the underlying pathological mechanisms is imperative.

Preclinical tumour-bearing models, together with dedicated models of chemotherapy-induced cardiotoxicity, now offer a unique opportunity to dissect tumour-driven versus treatment-related mechanisms of cardiac cachexia by isolating the effects of cancer burden from those of specific agents. These systems enable detailed investigation of inflammatory, metabolic and proteolytic pathways that are difficult to resolve in heterogeneous clinical populations. Moreover, these models permit systematic evaluation of cachexia-targeted interventions under controlled conditions.

With growing insight into the mechanisms driving cancer-associated cardiac cachexia, the early identification and longitudinal monitoring of cardiac wasting have become critical components of clinical care, with the potential to preserve cardiovascular function, enhance quality of life and improve long-term prognosis in patients with cancer.

This review provides a comprehensive overview of the principal mechanisms of cancer-related cardiac wasting, focusing on the molecular and cellular pathways involved in its pathogenesis. We also highlight the clinical implications of cancer-related cardiac wasting for morbidity, mortality and quality of life. We then discuss current diagnostic strategies, including both conventional and emerging imaging techniques and biomarkers that may allow for earlier, more accurate detection. Furthermore, we explore potential preventive and therapeutic interventions to mitigate cardiac damage, preserve cardiac function and ultimately improve long-term cardiovascular outcomes in oncologic populations. By integrating basic science with clinical evidence, this review aims to support the development of more effective cardio-oncologic strategies.

2 | DEFINITION AND CLARIFICATION OF CARDIAC WASTING

Cardiac wasting is defined as loss or atrophy of heart muscle in patients affected by chronic disease such as advanced-stage cancer, heart failure (Lena, Ebner, & Anker, 2019) and chronic obstructive pulmonal disease (Vonk-Noordegraaf, 2010). This process is part of the systemic syndrome of cachexia, which is characterized by weight loss, muscle atrophy and metabolic disturbances. In fact, particularly small hearts have been observed in cachectic patients with cancer (Barkhudaryan et al., 2017; Lena et al., 2023). However, cardiac wasting specifically implicates morphologic remodelling and functional changes within the heart. Structurally, this involves a marked reduction in the internal dimensions and wall thickness of the ventricles, leading to a significant loss of cardiac mass.

The progressive loss of myocardial mass and structural integrity constitutes a ‘shrinking’ phenomenon that often impairs cardiac performance, which can clinically mimic heart failure (Lena et al., 2023). Although cardiac functional decline has been observed even in the absence of pre-existing cardiovascular disease (CVD) or prior exposure to cardiotoxic cancer treatments (Lena et al., 2023), the underlying causality remains incompletely understood and current evidence suggests a distinct but not yet fully elucidated pathophysiological process. Patients may present with typical signs and symptoms of heart failure, such as fatigue, dyspnoea and exercise intolerance, despite preserved ejection fraction and no apparent ischaemic or hypertensive heart disease (Anker, Rashid, Butler, & Khan, 2025). This underscores the need to consider cancer-related cardiac wasting as an independent contributor to cardiac dysfunction in patients with cancer, warranting specific diagnostic attention and tailored clinical management.

An overview of the various preclinical and clinical studies investigating cancer-induced cardiac wasting is provided in Tables 1 and 2. Taken together, these data illustrate that currently available preclinical models of cancer-associated cardiac cachexia only partially mirror the spectrum of cardiac remodelling patterns described in patients. Many tumour-bearing mouse models develop rapidly progressive disease, in young otherwise healthy animals, and may show different remodelling markers like left ventricle dilatation or myocardial oedema that differ from the reduced ventricular volumes and subtle myocardial thinning reported in clinical cohorts. This makes it challenging to capture the chronic and heterogeneous manifestations of human cardiac wasting. In addition, commonly used tumour types, implantation sites and immunodeficient host strains do not fully recapitulate human tumour biology, systemic inflammation or multimorbidity. Harmonized diagnostic assessments are also frequently lacking, which may contribute to discrepancies between cardiac-wasting phenotypes observed in animal studies and the less impacting cardiac findings emerging from clinical datasets. The relative paucity of preclinical studies specifically addressing cardiac wasting over the last decade likely reflects the technical demands of modelling chronic tumour-mediated cardiac atrophy, which requires long-term tumour-bearing models, repeated high-quality cardiac phenotyping and careful distinction from cachexia of other organs. Finally, the heterogeneity of tumour entities and host

TABLE 1 Overview of cardiac wasting—Preclinical evidence.

Publication	Year	Key finding	Cancer type/model	Study subject
Tian et al. (2010)	2010	Heart weight ↓ 21% in tumour-bearing mice vs. controls	Colon-26 adenocarcinoma	Mice
Zhou et al. (2010)	2010	Heart weight ↓ 26%–29% in tumour-bearing mice vs. controls	Inhibin-α KO (gonadal tumour) Colon-26 adenocarcinoma	Mice
Cosper & Leinwand (2011)	2011	Cardiac mass loss: ∼10% (female), ∼22% (male) at day 27	Colon-26 adenocarcinoma	Mice
Manne et al. (2013)	2013	Cardiac mass loss: 8% at 12 weeks and 6% at 20 weeks of age	ApcMin/+ colorectal cancer	Mice
Palus et al. (2013)	2013	Heart weight ↓ 34% in tumour-bearing mice vs. controls	Yoshida AH-130 hepatoma	Rats
Hinch et al. (2013)	2013	Heart weight ↓ 24% in tumour-bearing mice with CC vs. controls, heart weight ↓ 19% in tumour-bearing mice without CC vs. controls	Adenocarcinoma cells 13 and 16 (colon)	Mice
Springer et al. (2014)	2014	Up to 58% cardiac mass loss at Day 13	Yoshida AH-130 hepatoma	Rats
Schafer et al. (2016)	2015	Cardiac mass loss: 14% at 14 weeks of age	ApcMin/+ colorectal cancer	Mice
Schafer et al.	2015	Cardiac mass loss: 14% at Day 21	Colon-26 adenocarcinoma	Mice
Lee et al. (2021)	2021	Heart weight ↓ ∼10% vs. controls	Lewis lung carcinoma	Mice
Ogilvie et al. (2024)	2024	Heart weight ↓ ∼10%, with reductions in LV, RV and atrial mass	Ovarian cancer	Mice

Abbreviations: CC, cancer cachexia; LV, left ventricle; RV, right ventricle.

TABLE 2 Overview of cardiac wasting—Clinical evidence.

Publication	Year	Key finding	Cancer type/model	Study subject
Springer et al. (2014)	2014	Heart weight ↓ 25.6% in cancer patients with cachexia	NSCLC, GI cancer, pancreatic carcinoma	26 post-mortem patients
Cramer et al. (2014)	2014	No significant LVMI difference vs. controls	Colorectal cancer	50 patients
Barkhudaryan et al. (2017)	2017	Heart weight ↓ 19% in CC vs. cancer without CC and ↓ 12% vs. control group	Lung, pancreas, GI carcinoma	117 post-mortem patients
Kazemi-Bajestani et al. (2019)	2019	Median LV mass loss of 8.9% over 112 days	NSCLC	50 patients
Lena et al. (2023)	2023	LV mass ↓ 23% in cancer patients vs. controls; LV mass ↓ 24% in patients with CC. LV mass loss 9.3% over ∼4 months	Various cancer types	300 patients
Calamelli et al. (2023)	2023	Cachectic patients: ↓ LV wall thickness & septum; no significant LV mass difference	Head & neck cancer	42 patients

Abbreviations: CC, cancer cachexia; GI, gastrointestinal; LV, left ventricular; LVMI, left ventricular mass index; NSCLC, non-small cell lung cancer.

backgrounds further complicates standardization, which may have slowed the broader implementation of dedicated cardiac-wasting models.

In parallel, clinical awareness of cardiac wasting in cancer has grown recently, thanks to large imaging cohorts and prospective echocardiography studies that could opportunistically quantify left ventricular mass and function in unselected oncology populations, leading to several new clinical reports in the 2010s–2020s without the need for dedicated animal work.

3 | PATHOPHYSIOLOGY OF MALIGNANCY-ASSOCIATED CARDIAC WASTING

Although the pathophysiological background of cardiac wasting in cancer is deeply interconnected with systemic cachexia, specific key features can be identified (Lena, Ebner, Coats, & Anker, 2019). The pathogenesis of this tumour-related cardiac wasting involves metabolic disturbances, inflammation, proteolytic dysregulation and

neurohormonal dysfunctions (Figure 1). These mechanisms (Lena et al., 2021) represent specific targets for a novel therapeutic strategy against cardiac-wasting associated cardiomyopathy.

3.1 | Cancer cachexia

Cachexia is characterized by an irreversible loss of at least 5% of body mass within 6 months, predominantly involving lean mass, whereas fat loss varies (Fearon et al., 2011). Notably, cachexia may be concealed in cases of concurrent obesity, where fat accumulation masks the loss of lean tissue (Dahlman et al., 2010). Cachexia affects up to 80% of patients with metastatic cancer and represents a leading tumour-associated cause of death in about one-third of patients with cancer (Dunne et al., 2024; Mariean et al., 2023). Muscle loss is observed to be the hallmark in cancer cachexia (Hadzibegovic et al., 2023; Ishida et al., 2017). It is induced by an up-regulation of proteolytic pathways in the muscle tissue. This is driven by factors secreted by tumour-, metastases- and activated immune cells (Setiawan et al., 2023). The adipose tissue is also targeted by the systemic catabolic impairment acting in cancer cachexia. In this case, lipolysis is associated with other pro-cachectic mediators. For example, zinc-alpha-2-glycoprotein (ZAG), also known as lipid mobilizing factor (LMF), performs a lipolytic action in white adipose tissue (Bing et al., 2004).

3.2 | Inflammation

One of the main driving factors responsible for wasting processes is a widespread pro-inflammatory state in cancer (Baracos et al., 2018). Increased levels of interleukins (IL), such as IL-1 and **IL-6** (Rupert et al., 2021; Tian et al., 2010); **tumour necrosis factor (TNF)** (Beutler & Cerami, 1986); and **transforming growth factor family-beta (TGF-β)** (Balsano et al., 2022) have been variously reported in cancer models and cancer populations. These pro-inflammatory cytokines, produced by immune cells in response to cancer, promote protein degradation directly and through paracrine signalling mediated by tumour-associated stromal and immune cells.

Proinflammatory cytokines induce cardiac cachexia at different levels. IL-6 (Tanaka et al., 2004) and TNF (Anker, Rashid, Butler, & Khan, 2025) impair cardiac metabolism by reducing fatty acid oxidation and mitochondrial function. This leads to a metabolic down-regulation and an atrophic cardiac phenotype in cancer (Garcia-Garduño et al., 2021). TNF also activates intracellular pathways such as **nuclear factor kappa-light-chain-enhancer of activated B-cells (NF-κB)**, enhancing proteolysis via the ubiquitin–proteasome and autophagy–lysosome systems while suppressing protein synthesis (Vudatha et al., 2022). Inflammation, primarily through TGF-β signalling, drives cardiac remodelling and fibrosis (Saha et al., 2022). Interestingly, cardiac fibrotic changes have been observed independently of skeletal muscle cachexia (Springer et al., 2014). This suggests that

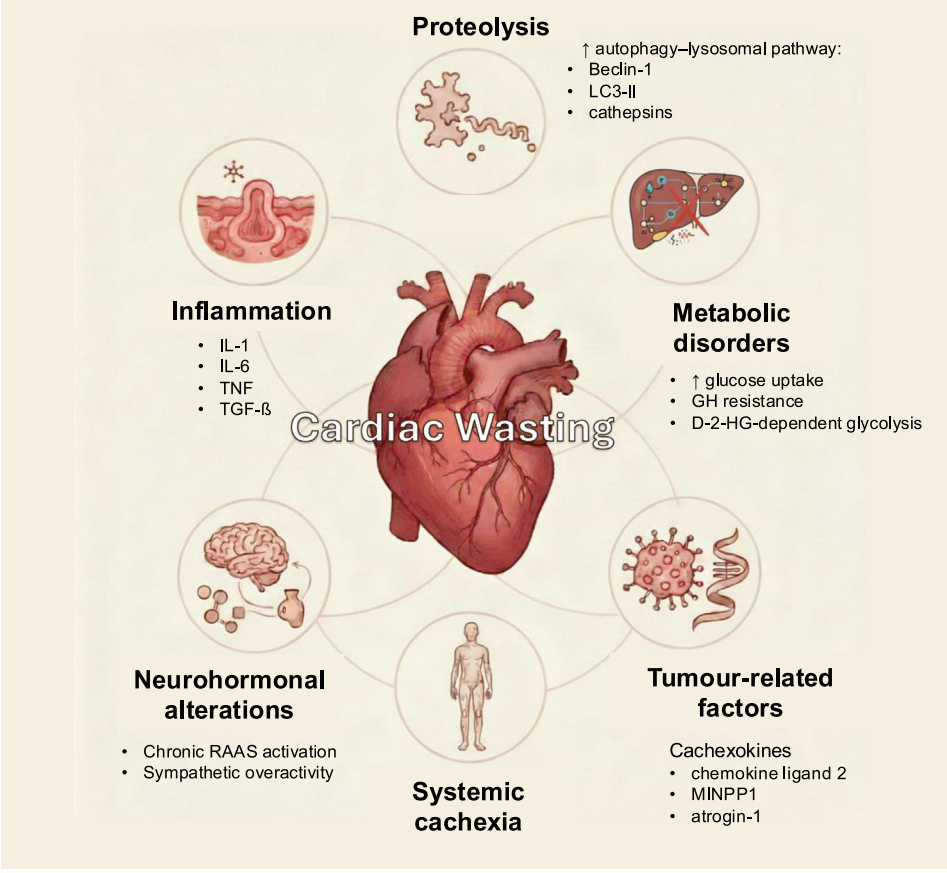

FIGURE 1 Proposed pathophysiologic mechanisms of cardiac wasting in cancer.

local inflammation also contributes to cardiac remodelling. Chronic inflammation further inhibits anabolic pathways, including **insulin growth factor-1 (IGF-1)**/**protein kinase B (Akt)**, **mechanistic target of rapamycin kinase (mTOR)** signalling (Manne et al., 2013; Tichy & Parry, 2023) and exacerbates oxidative stress (Hinch et al., 2013). Ultimately, a hyperactivated inflammatory status is associated with increased autophagy and apoptosis in cardiomyocytes (Cosper & Leinwand, 2011; Gunadi et al., 2021), leading to cell loss and functional decline.

Elevated expression of pro-inflammatory cytokines in the myocardium of rodent models with cancer cachexia supports this hypothesis (Ogilvie et al., 2024; Rupert et al., 2021). These findings suggest that tumour growth, by inducing a systemic pro-inflammatory state, can causally and directly contribute to cardiac injury, and subsequent dysfunction, independently from other factors like cancer therapies. This concept is further reinforced by recent *in vitro* studies demonstrating cardiomyocyte damage in the concurrent presence of cancer cells (Buoncervello et al., 2019).

3.3 | Metabolic alterations

Cancer cachexia is characterized by various metabolic disturbances and a resulting catabolic phenotype. Since mitochondria generate 90% of the body's energy generation, many of these alterations are driven by a significant decline in mitochondrial function (Chen & Zweier, 2014). Given the fact that the cardiac muscle demands high energy (Lopaschuk et al., 2021), systemic metabolic disturbances in cachexia may also significantly contribute to the development of cachexia-related cardiomyopathy. To date, data about metabolic dysregulation of the cardiac tissue in the presence of cancer are controversial.

Cardiac energy regulation and contractile function are highly dependent on fatty acid oxidation, whereas a small amount of energy comes from the oxidation of glucose and lactate (Wisneski et al., 1987). Preclinical studies adopting C26 tumour-bearing mouse models reported a metabolic switch to a preferential glucose absorption in the presence of cancer (Tian et al., 2010). This is driven by changes in gene expression, including reduced expression of **peroxisome proliferator-activated receptor alpha (PPARα/NR1C1)**, and a shift in myosin heavy chain (MHC) isoforms from an 'adult' to an 'embryonic' profile. Evidence of increased glucose uptake in the cardiac tissue, independently from the presence of systemic cachexia, has been recently reported also in patients affected by Hodgkin's lymphoma (Heckmann et al., 2019). This increased pathological energy demand, in conjunction with restricted capacity for energy production, may be responsible for structural remodelling and associated impaired cardiac function.

Conversely, **insulin** deficiency has been detected in cachectic tumour-bearing mice (Asp et al., 2010) as well as in cancer patients (Copeland et al., 1987; Raun et al., 2022). In different mouse models, the resulting insulin depletion inhibits cellular glucose uptake (Drott & Lundholm, 1990). In this scenario, the reduced glucose oxidation in the cardiac tissue was associated with cardiac dysfunction, supporting the hypothesis that a reduced metabolism may induce cardiac atrophy and consequent aberrant contractile function. Nevertheless, it has been proven that insulin injection may help mitigate this cardiometabolic disruption by restoring a regular insulin signalling in the cardiomyocytes (Thackeray et al., 2017).

Additionally, other metabolic alterations involving the growth hormone (GH) axis have been observed in cancer cachexia (Bing, 2005; Trobec et al., 2011) and cancer-induced cardiac wasting (Fröhlich et al., 2024). The growth hormone is a pituitary peptide hormone that stimulates cellular growth (especially of bone and cartilage) and promotes protein anabolism. In adults, it also helps regulate body composition and metabolism by increasing lipolysis and influencing glucose handling via **insulin-like growth factor-1 (IGF-1**; (Fröhlich et al., 2024). A disruption in the growth hormone-axis is associated with a form of growth hormone resistance characterized by reduced growth hormone receptor or growth hormone-binding protein levels, increased growth hormone levels in the blood and low IGF-1 levels. A down-regulation of IGF-I, which normally supports the cardiomyocytes survival by inhibiting cell death, may contribute to the development of apoptotic processes in the cardiac muscle.

The oncometabolite D2-hydroxyglutarate (D2-HG), produced aberrantly by cancer cells, may mediate a direct and maladaptive crosstalk in the cardiac tissue. Recent studies (Karlstaedt et al., 2021) show that elevated levels of D2-hydroxyglutarate can impair cardiac metabolism by inhibiting α-ketoglutarate dehydrogenase, causing metabolic reprogramming that includes impaired oxidative phosphorylation and a shift towards glycolysis in cardiomyocytes. D2-hydroxyglutarate promotes contractile dysfunction, reduced cardiac power and altered energy substrate utilization. It also induces epigenetic changes such as histone modifications in cardiac tissue that further contribute to cardiac dysfunction. In the context of cancer cachexia, D2-hydroxyglutarate accumulation has been linked to skeletal muscle atrophy and metabolic disturbances affecting the heart, making it a novel metabolic mediator of cardiac wasting in cancer (Karlstaedt et al., 2016).

Given these diverse metabolic alterations and different models of cardiometabolic inefficiency in cancer-induced cardiomyopathy, further research is required to clarify the underlying pathological mechanisms. In particular, it is increasingly important to determine whether this metabolic shift occurs independently or is driven mainly by the development of systemic cachexia and tumour progression.

3.4 | Proteolysis

The cardiac wasting characteristic of cancer-induced cachexia arises from a combination of accelerated protein degradation and impaired protein synthesis. Although three major proteolytic routes have been described in systemic cachexia, the ubiquitin–proteasome system (UPS) (Delfinis et al., 2022), calcium-activated proteases (Law & Metzger, 2021) and autophagy (Sandri, 2016), current evidence suggests that the autophagy–lysosomal pathway assumes a particularly dominant role in the heart, distinguishing cardiac from skeletal muscle

wasting in the context of cancer. Concurrently, the suppression of anabolic signalling through the Akt/mTOR pathway further limits cardiac protein renewal and regeneration (Manne et al., 2013).

Multiple studies in tumour-bearing animals have documented a significant up-regulation of autophagic mechanisms in cardiac muscle (Cosper & Leinwand, 2011; Musolino et al., 2016). Specifically, elevated levels of autophagy markers, including beclin-1, microtubule-associated protein 1 light chain 3 (LC3-II) and lysosomal enzymes such as **cathepsins**, reflect an increased autophagosome formation and enhanced lysosomal degradation activity within cardiomyocytes (Ogilvie et al., 2024). In contrast, the role of the UPS in cancer-induced cardiac wasting is less prominent and controversial. Although some studies associate protein breakdown in cardiac wasting with UPS-mediated pathways (Ding et al., 2017; Springer et al., 2008; Springer et al., 2014; Tian et al., 2011), others have failed to corroborate these findings. For example, an ovarian cancer model showed no significant increase in the cardiac expression of muscle-specific ubiquitin ligases atrogin-1 and muscle RING-finger protein-1 (MuRF1) (Ogilvie et al., 2024). This indicates that UPS involvement may be context-dependent, varying with cancer type, and points to a potentially secondary role for this pathway in cancer-induced cardiac wasting.

3.5 | Neurohormonal disturbances

Neurohormonal dysfunction, mainly involving the renin–angiotensin–aldosterone system (RAAS) and the sympathetic nervous system (SNS) signalling, contributes to cardiac wasting in cancer, with supporting roles from adrenal axis disruption. Patients and mice with cancer-induced cardiac wasting show elevated plasma **renin**, **aldosterone** and **noradrenaline**, reflecting heightened RAAS and sympathetic nervous system activity (Springer et al., 2014). Chronic RAAS activation promotes vasoconstriction, myocardial fibrosis, inflammation, oxidative stress and increased wall stress, mainly through the **angiotensin II–AT_1 receptor** pathway (Garcia-Garduño et al., 2021). Elevated aldosterone is associated with cardiac fibrosis and ventricular thinning, whereas both clinical and experimental data confirm that renin and aldosterone increase in advanced cancer, driving cardiac remodelling. For example, serum aldosterone and renin levels were elevated in patients with cachexia by 2.1-fold and 2.9-fold, respectively (Springer et al., 2014). Sympathetic overactivity further elevates catecholamines, worsening myocardial catabolism and apoptosis (Ogilvie et al., 2024). Moreover, a hyperregulated adrenal axis, characterized by adrenal gland hypertrophy and increased cortisol in cancer models, promotes fibroblast activation, adverse cardiac remodelling and the development of an arrhythmogenic substrate in cardiac atrophy (Anker et al., 2020).

3.6 | Other tumour-related factors

Cancer initiates a cascade of systemic and myocardial inflammatory and metabolic disturbances that drive cachexia, contributing to cardiomyocyte atrophy, metabolic dysfunction and fibrotic remodelling in the heart (Anker, Rashid, Butler, & Khan, 2025). The cancer site/entity can also influence the cachexia phenotype and induce cardiac wasting in a different measure (Matsuyama et al., 2015). Direct tumour-related factors include a range of secreted proteins (cachexokines) like chemokine ligand 2 (Iaia et al., 2025) and multiple inositol-polyphosphate phosphatase 1 (MINPP1) (Yu et al., 2023). These mediators contribute to muscle wasting and dysfunctional fatty acid oxidation in cardiomyocytes. Ataxin-10, a non-inflammatory protein mainly associated with the survival of spinocerebellar cells, has been studied in the C26 adenocarcinoma model (Schafer et al., 2016). Elevated levels of ataxin-10 were associated with cardiac atrophy in murine models as well as in patients with pancreatic cancer, defining a novel diagnostic biomarker for cardiac wasting in cancer.

4 | CLINICAL IMPLICATIONS

4.1 | Risk factors

Although the precise pathological mechanisms of malignant cardiac wasting remain under investigation, several clinical risk factors have been identified. Certain cancer types, such as lung, pancreatic and gastrointestinal malignancies, are more strongly linked with systemic cachexia, making patients with these conditions also more susceptible to developing cardiac wasting.

Gastrointestinal cancers are often associated with symptoms such as loss of appetite, difficulty eating and malabsorption. These issues contribute to malnutrition, which in turn accelerates the systemic catabolic shift, as the lack of adequate nutrient intake further worsens energy and protein deficiencies, similar to what is observed in cardiac cachexia (von Haehling et al., 2007). Indeed, nutritional deficiency has been linked to a loss of heart weight in both cancerous and non-cancerous rat models (Drott et al., 1986). More recent data confirm that patients with cardiac wasting across various cancer types have a heightened risk of malnutrition (Lena et al., 2023).

Anti-cancer treatments also pose a risk for cardiac toxicity, either directly via myocardial damage or indirectly via local inflammation and immune dysregulation. For example, an association between anthracyclines and heart weight reduction has been observed (Cove-Smith et al., 2014; Moulin et al., 2015). Cardiac dysfunction further amplifies the risk of cardiac wasting (Asnani, 2023). However, recent studies suggest that cardiac wasting may occur independently of chemotherapy (Lena et al., 2023), indicating that atrophy and fibrotic processes may be driven by the tumour itself. Once the tumour progresses, the wasting process begins, with anti-cancer treatments potentially exacerbating the condition.

Reduced physical activity is also crucial in the prevention of skeletal and cardiac atrophy. Sedentary behaviour in tumour-bearing mice leads to pronounced loss of lean and fat mass, diminished cardiac function and increased expression of muscle-wasting markers such as atrogin1, muscle RING-finger protein-1 (MuRF1), growth differentiation factor 15 (GDF15) and **GDF8**/**GDF11** in the heart (Tichy

et al., 2025). Diminished physical performance is more pronounced in patients with cardiac wasting than in those with preserved cardiac mass (Lena et al., 2023).

Finally, patient-inherent individual factors also represent relevant risk factors. Advanced age and the presence of comorbidities, particularly chronic cardiac and metabolic diseases, significantly exacerbate both the risk and severity of cancer-associated cardiac wasting. Both cancer and CVDs are more common in older adults, and the combination of age-related cardiovascular changes, chronic inflammation (often referred to as 'inflammaging') and a higher incidence of cancer heightens the risk of cardiac complications, including cardiac wasting (Anker, Rashid, Butler, & Khan, 2025). These factors interact by amplifying systemic inflammation, disrupting metabolic processes and increasing cardiac vulnerability within this population (Ioffe et al., 2024).

4.2 | Clinical presentation and diagnostics

The clinical presentation of cardiac wasting in patients with cancer usually combines general cachexia manifestations with cardiac-specific signs (Anker et al., 2020; Anker et al., 2024). Typical heart failure symptoms such as exertional dyspnoea, orthopnoea, peripheral oedema and fatigue indicate cardiac dysfunction. These often coexist with systemic features of cachexia, including fatigue, weight loss, malaise, night sweats and loss of appetite, which reflect ongoing metabolic derangements and chronic inflammation. In addition, arrhythmias and conduction abnormalities may occur as consequences of malignant cardiac remodelling (Albrecht et al., 2021). This clinical presentation refers to a peculiar phenotype, recently described as cardiac-wasting associated cardiomyopathy (Lena et al., 2023).

A multimodal diagnostic approach represents the most effective strategy for early detection of cancer-induced cardiac wasting. Echocardiography remains the first-line tool, enabling assessment of structural remodelling and functional parameters such as left ventricular ejection fraction (LVEF); global longitudinal strain (GLS), used to measure the shortening of longitudinal myocardial fibres; and diastolic function. When results are inconclusive or a more detailed evaluation is required, cardiac magnetic resonance imaging (CMR) provides superior resolution for myocardial morphology, tissue characterization (including fibrosis via late gadolinium enhancement) and ventricular performance (Čelutkienė et al., 2020).

Alongside imaging, circulating serum biomarkers play a central role. Inflammatory markers, such as C-reactive protein (CRP), TNF and IL-6, are consistently elevated in cancer cachexia and strongly linked to muscle wasting, including cardiac atrophy. Cardiac stress markers, including **brain natriuretic peptide (BNP)**, N-terminales pro-BNP (NT-proBNP), midregional proadrenomedullin (MRproADM) and cardiac troponins, may predict cardiac involvement before overt dysfunction becomes clinically evident (Anker, Lück, Khan, Porthun, Hadzibegovic, et al., 2025; Lyon et al., 2020; Pudil et al., 2020). Emerging cardiac-specific biomarkers include autophagy-related markers such as beclin-1, LC3 (with LC3-II accumulation indicating enhanced autophagic flux) and lysosomal proteases (cathepsin L and D), which have been shown to be up-regulated in cachexia models (Cosper & Leinwand, 2011). Despite the secondary role of proteolysis in cancer-induced cardiac atrophy, atrogin-1 (Hosny et al., 2025; Pietzsch et al., 2020) and muscle RING-finger protein-1 (MuRF1) have been found to be up-regulated in some preclinical studies (Bagnall et al., 2023). Additional cytokines, including **IL-1β** and **IL-10**, may further contribute to inflammation-driven cardiac remodelling and wasting (Tichy & Parry, 2023).

4.3 | Prognostic impact

Cardiac wasting in cancer significantly impairs cardiac function; as a compensatory mechanism to a shrinking and atrophic cardiac muscle, resting heart rate rises and stroke volume diminishes (Anker, Khan, Nikolski, Porthun, Arshad, et al., 2025; Lena et al., 2023). In addition, there is evidence that global longitudinal strain, a measurement of myocardial longitudinal deformation of the left ventricle (LV) during contraction, is also impaired in atrophic hearts (Kazemi-Bajestani et al., 2019; Lena et al., 2023). These alterations could explain some of the similarities to heart failure syndrome. The quality of life is also compromised due to cardiac inefficiency. A recent multimodal analysis of patients suffering from different cancer types demonstrated an association of reduced physical performance, muscle strength and risk of malnourishment in patients with malignant cardiac wasting in comparison with individuals with preserved cardiac mass (Lena et al., 2023).

Cancer-associated cardiac wasting is an adverse prognostic factor, with one-year mortality rates exceeding 40% in some cancer patients (Lena et al., 2023). Importantly, this association is observed regardless of exposure to cardiotoxic cancer therapies, underscoring cardiac wasting as a prognostic biomarker that reflects the severity of systemic cachexia and overall tumour burden (Lena et al., 2023).

5 | THERAPEUTIC APPROACHES AND MANAGEMENT

Despite well-documented clinical and prognostic implications, malignant cardiac wasting remains an unmet therapeutic target in oncology. A major challenge lies in its profound interconnection with systemic processes, including cancer-associated cachexia, chronic inflammation, metabolic imbalance and neurohormonal dysregulation, that act synergistically to drive disease progression. This complex interplay obscures the distinction between cardiac and systemic manifestations, making it difficult to identify specific therapeutic targets and to develop effective treatments (Figure 2).

5.1 | Pharmacological experiences

Pharmacological ideas on how to counteract cancer-induced cardiac wasting in the future largely rely on repurposing well-established

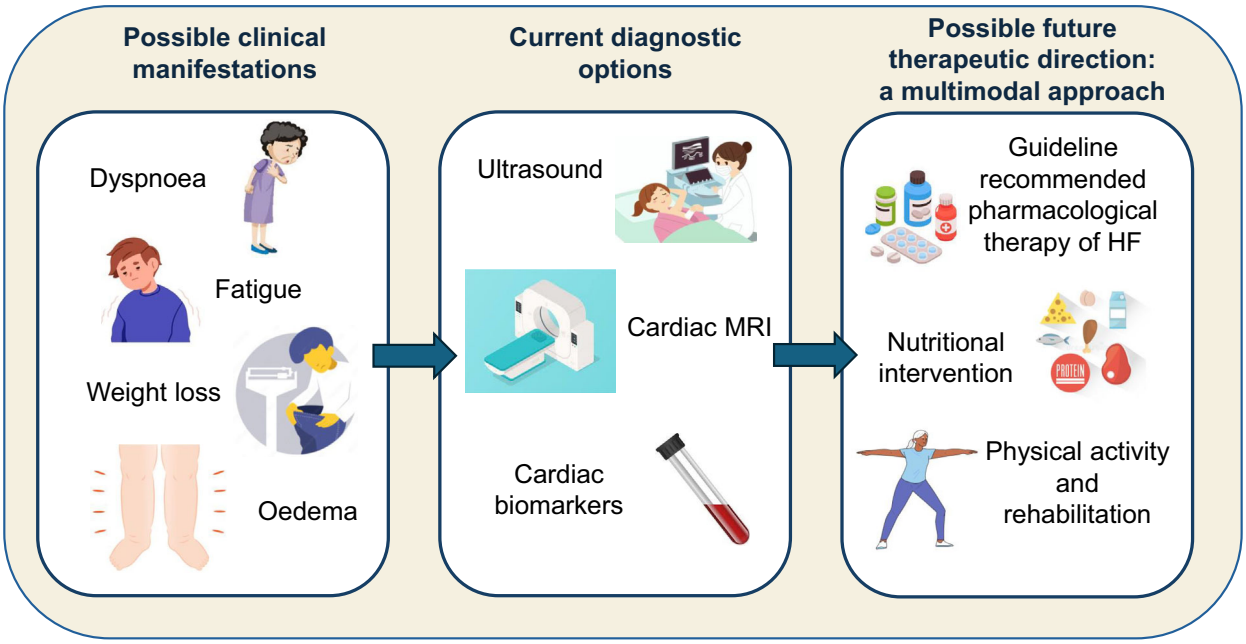

FIGURE 2 Workflow in cancer-related cardiac wasting.

heart failure therapies to mitigate adverse remodelling and preserve cardiac function (Anker, Rashid, Butler, & Khan, 2025; Vudatha et al., 2022). This therapeutic strategy is mainly based on preclinical evidence of heart failure therapy to prevent and counteract cardiotoxic-induced cardiomyopathy (Contaldi et al., 2025).

Different heart failure treatments in animal models, however, have yielded different results. For example, although **imidapril** attenuated cardiac dysfunction and wasting in tumour-bearing mice likely through improved endothelial function, modulation of IGF-1 and suppression of pro-inflammatory cytokines, it failed to improve survival (Springer et al., 2014). Similar benefits have been observed with angiotensin 1-receptor antagonists, where **losartan** preserved systolic function and restricted ventricular remodelling in C26 tumour models (Stevens et al., 2015). **Mineralocorticoid receptor** antagonists and beta blockers have also demonstrated survival advantages and preservation of cardiac mass, though bisoprolol did not enhance systolic function in preclinical models (Springer et al., 2014). These cardioprotective effects appear linked to restoration of signalling pathways governing cell growth and survival rather than targeting proteolytic and autophagic processes in the myocardium.

The recently published EMPATICC trial evaluated whether an optimized heart failure regimen (randomizing **sacubitril/valsartan**, **empagliflozin**, **ivabradine** and ferric carboxymaltose vs. placebo) could improve functional capacity and quality of life in patients with advanced cancer and increased cardiovascular risk (Anker, Bercker, Laufs, Böhm, Merkely, et al., 2025; Anker, Mahabadi, Totzeck, Tewes, Mincu, et al., 2025a; Anker, Mahabadi, Totzeck, Tewes, Shahzeb Khan, et al., 2025b). Its combined primary endpoint focused on measures of self-care ability, walking performance and overall well-being but was not significant during 30 days of follow-up. However, the therapy positively influenced secondary endpoints such as left ventricular ejection fraction (LVEF +2.9%), NTproBNP (−41%) and patient global assessment at Day 30. EMPATICC represents one of the first rigorous proof-of-concept randomized controlled trials specifically addressing heart failure (HF)-like syndromes in patients with terminal cancer, shifting the focus from merely managing therapy-related cardiotoxicity to directly targeting cancer-associated cardiac wasting. Nonetheless, further high-quality clinical trials are urgently needed to confirm these findings and to establish evidence-based treatment strategies.

In parallel, preclinical research has focused on targeting molecular pathways that drive cachexia and cardiac atrophy, including systemic inflammation and proteolytic mechanisms. TNF has been one of the first studied pharmacological targets in murine models. Anti-TNF treatment in tumour-bearing rats mitigated protein degradation in cardiac muscle (Costelli et al., 1993). In addition, inhibition of cardiac **NF-κB** activity showed promise against cardiac muscle loss (Wysong et al., 2011). Experimental approaches have also explored modulators of the UPS and myostatin/activin signalling (Toledo et al., 2016). Specifically, inhibiting the myostatin/activin pathway via **activin A receptor type 2B (ActRIIB)** blockade or neutralizing antibodies has been shown to reverse or attenuate muscle and cardiac wasting in various animal models of cancer cachexia (Zhou et al., 2010).

Nevertheless, these experiences remain limited to animal models and have not been investigated in humans. The majority of ongoing clinical trials prioritize systemic cachexia and preservation of lean body mass as their primary therapeutic endpoints (Crawford et al., 2023). Promising preclinical drugs (e.g. **withaferin A**, **mitogen-activated protein kinase 1 [MEK1]** and **2 [MEK2]** and NFκB

modulators) now require validation in human trials (Saha et al., 2022). To date, no approved therapies specifically target malignant cardiac wasting, likely because cardiac muscle loss is most often assessed only as a secondary outcome. This underscores a critical gap in translational research and highlights an important unmet clinical need.

5.2 | Metabolic interventions and nutritional support

Metabolic dysregulation has been recently detected as an additional therapeutic target (Karlstaedt et al., 2022). In particular, the degradation of cardiolipin, an essential mitochondrial phospholipid and disturbed linoleic acid metabolism are emerging as crucial contributors to cardiac atrophy in the setting of cancer cachexia. Nutritional interventions and drugs modifying fatty acid metabolism, mitochondrial stability or oxidative stress pathways are actively being researched as strategies to halt or delay metabolic cardiac wasting associated with cancer (Wang et al., 2024). Promising findings are reported by Palus et al. (Palus et al., 2013) on the use of statin therapy in tumour-bearing rats. Treatment with simvastatin led to a reduction in both systemic and cardiac wasting, accompanied by improved cardiac function. Overall, simvastatin therapy enhanced survival in cancer models. These beneficial effects are likely mediated by the anti-inflammatory properties of statins, potentially through the reduction of low-density lipoprotein levels. In contrast, the antidiabetic drug **rosiglitazone** was associated with a reduction of body wasting and improved cardiac function but did not show any effect on cardiac weight in the same animal model (Trobec et al., 2014).

5.3 | Physical activity and rehabilitative measures

Exercise confers multifaceted benefits in the setting of cancer by mitigating myocardial inflammation, oxidative stress, fibrotic remodelling and metabolic derangements (Belloum et al., 2017). Regular aerobic training reduces circulating inflammatory cytokines and enhances endogenous antioxidant defences, thereby counteracting inflammation-driven pathways that contribute to cardiac autophagy and atrophy in cancer cachexia (Parry et al., 2022; Parry & Hayward, 2018). In addition, aerobic exercise helps preserve IGF-1/**phosphatidylinositol 3-kinase** and **protein kinase B** (**PI3K/Akt**) signalling, supporting physiological cardiac hypertrophy and maintaining contractile performance (Belloum et al., 2017). Endurance exercise further improves oxidative metabolism by stimulating mitochondrial biogenesis and increasing mitochondrial protein content in cardiac tissue (Belloum et al., 2017). Importantly, these preclinical findings translate into clinical relevance, as improved cardiorespiratory fitness through structured physical activity has been associated with better survival outcomes in patients with colorectal cancer (Courneya et al., 2025). Taken together, these data highlight the importance of early identification of patients at high risk of developing systemic wasting, who may benefit most from targeted exercise interventions, in combination with potential pharmacological treatments.

6 | CONCLUSION AND OUTLOOK

Addressing cancer-related cardiac morbidity and particularly cardiac wasting has gained momentum and established a promising area of future research, given its profound consequences on quality of life and survival. To clinically impact on patients, a paradigm shift of the current understanding of cardiac wasting in cancer patients is needed, moving the topic from late a complication-recognition in towards early surveillance and consecutively a proactive therapeutic intervention. Standardized methods to quantify cardiac mass loss and validated biomarkers capable of identifying subclinical cardiac wasting will be key to enabling timely therapy. Such markers should not only reflect disease biology but also predict treatment response and clinical benefit.

Future therapeutic strategies should aim not only to preserve skeletal muscle mass but also to directly target cardiac muscle wasting, with the goal of improving cardiorespiratory fitness, functional independence and physical activity levels—factors that could ultimately reduce mortality in this vulnerable population both directly on a cardiac function level as well as indirectly by improving therapeutic adherence in patients undergoing systemic therapy. This will likely require identifying novel pharmacological targets specific to cardiac muscle, focusing on pathways that limit autophagy and regulate hypertrophy, mitochondrial health and contractile function, in order to restore myocardial performance.

In the short term, repurposing established heart failure therapies that attenuate neurohormonal activation, such as inhibition of the RAAS and sympathetic signalling, represents a practical strategy to mitigate cancer-associated cardiac atrophy. Several agents, including ACE inhibitors, beta-blockers (β-adrenoceptors antagonists) and mineralocorticoid receptor antagonists, have already demonstrated beneficial effects in preclinical models of tumour-bearing mice. Beyond this approach, more targeted interventions aimed at central catabolic and anabolic pathways in the cachectic myocardium, such as myostatin/activin signalling, the ubiquitin–proteasome and autophagy–lysosome systems and regulators of mitochondrial quality control, offer promising directions for future drug development. Moreover, clinical trials that combine these candidate therapies with structured exercise, nutritional and anti-inflammatory strategies, while incorporating cardiac endpoints into oncologic study designs, will be needed to determine whether modulation of these pathways can preserve cardiac structure, improve functional performance and ultimately enhance survival in patients with cancer.

Achieving this will require a more integrated cardio-oncology approach, fostering collaboration between oncologists, cardiologists and basic scientists, and embedding translational research within clinical care. The implementation of cardiac monitoring into

oncological treatment algorithms may represent a critical step towards transforming these mechanistic insights and therapeutic advances into improved outcomes for patients.

6.1 | Nomenclature of targets and ligands

Key protein targets and ligands in this article are hyperlinked to corresponding entries in the IUPHAR/BPS Guide to PHARMACOLOGY http://www.guidetopharmacology.org and are permanently archived in the Concise Guide to PHARMACOLOGY 2025/2026 (Alexander, Cidlowski, et al., 2025; Alexander, Gibb, et al., 2025).

AUTHOR CONTRIBUTIONS

Alessia Lena: Writing—original draft (lead); writing—review and editing (equal). **Muhammad Shahzeb Khan:** Writing—review and editing (equal). **Ulrich Keller:** Writing—review and editing (equal). **Lars Bullinger:** Writing—review and editing (equal). **Dominik P. Modest:** Writing—review and editing (equal). **Markus S. Anker:** Writing—original draft (supporting); writing—review and editing (equal).

CONFLICT OF INTEREST STATEMENT

M.S.K. has received consultancy fees or research support from Bayer, Novartis, Boehringer Ingelheim, and Merck. A.L., U.K., L.B., D.P.M. and M.S.A. declare no conflicts of interest.

ACKNOWLEDGEMENTS

Open Access funding enabled and organized by Projekt DEAL.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are openly available in Pubmed at https://pubmed.ncbi.nlm.nih.gov/.

REFERENCES

Albrecht, A., Porthun, J., Eucker, J., Coats, A. J. S., von Haehling, S., Pezzutto, A., Karakas, M., Riess, H., Keller, U., Landmesser, U., Haverkamp, W., Anker, S. D., & Anker, M. S. (2021). Spontaneous non-sustained ventricular tachycardia and premature ventricular contractions and their prognostic relevance in patients with cancer in routine care. *Cancers (Basel)*, *13*, 2303. https://doi.org/10.3390/cancers13102303

Alexander, S. P. H., Cidlowski, J. A., Gibb, A. J., Kelly, E., Mathie, A. A., Peach, C. J., Veale, E. L., Armstrong, J. F., Faccenda, E., Harding, S. D., Southan, C., Davies, J. A., Coons, L., Fuller, P. J., Korach, K. S., McDonell, D. P., Oakley, R., Radi, S., Safi, R., … Young, M. J. (2025). The concise guide to pharmacology 2025/26: Nuclear hormone receptors. *British Journal of Pharmacology*, *182*(Suppl 1), S242–S258. https://doi.org/10.1111/bph.70232

Alexander, S. P. H., Gibb, A. J., Kelly, E., Mathie, A. A., Peach, C. J., Veale, E. L., Cidlowski, J. A., Davenport, A. P., Fabbro, D., Spedding, M., Striessnig, J., Armstrong, J. F., Buneman, O. P., Faccenda, E., Harding, S. D., Southan, C., Davies, J. A., Ahlers-Dannen, K. E., Alqinyah, M., … Zolghadri, Y. (2025). The concise guide to pharmacology 2025/26: Introduction and other protein targets. *British Journal of Pharmacology*, *182*(Suppl 1), S1–S23. https://doi.org/10.1111/bph.70229

Anker, M. S., Bercker, S., Laufs, U., Böhm, M., Merkely, B., Diek, M., Heise, T., Hellmich, M., Placzek, M., Friede, T., Anker, S. D., Lehmann, L., Landmesser, U., Modest, D. P., Shahzeb Khan, M., Mahabadi, A. A., Totzeck, M., Tewes, M., Arshad, M. S., … Rassaf, T. (2025). Optimized heart failure therapy in patients with very advanced cancer in palliative care: Dosing strategies from the EMPATICC trial. *Global Cardiology*, *3*(3). https://doi.org/10.4081/cardio.2025.78

Anker, M. S., Khan, M. S., Nikolski, A., Porthun, J., Arshad, M. S., Hadzibegovic, S., Lena, A., Kretzler, L., Hella, J. L., Witkowski, M., Rieger, K., Ahn, J., Modest, D. P., Keller, U., Bullinger, L., Totzeck, M., Mahabadi, A. A., Rassaf, T., Buchmann, N., … Landmesser, U. (2025). Clinical and echocardiographic phenotype of cardiac wasting in patients with advanced cancer. *European Journal of Heart Failure*, *27*, 2130–2140. https://doi.org/10.1002/ejhf.3744

Anker, M. S., Lena, A., Roeland, E. J., Porthun, J., Schmitz, S., Hadzibegovic, S., Sikorski, P., Wilkenshoff, U., Fröhlich, A. K., Ramer, L. V., Rose, M., Eucker, J., Rassaf, T., Totzeck, M., Lehmann, L. H., von Haehling, S., Coats, A. J. S., Friede, T., Butler, J., … Ahn, J. (2023). Patient-reported ability to walk 4 m and to wash: New clinical endpoints and predictors of survival in patients with pre-terminal cancer. *Journal of Cachexia, Sarcopenia and Muscle*, *14*, 1670–1681. https://doi.org/10.1002/jcsm.13247

Anker, M. S., Lück, L. C., Khan, M. S., Porthun, J., Hadzibegovic, S., Lena, A., Wilkenshoff, U., Weinländer, P., Evertz, R., Totzeck, M., Mahabadi, A. A., Rassaf, T., Anker, S. D., Bullinger, L., Keller, U., Karakas, M., Landmesser, U., Butler, J., & von Haehling, S. (2025). New cardiovascular biomarkers in patients with advanced cancer—A prospective study comparing MR-proADM, MR-proANP, copeptin, high-sensitivity troponin T and NT-proBNP. *European Journal of Heart Failure*, *27*, 1047–1055. https://doi.org/10.1002/ejhf.3497

Anker, M. S., Mahabadi, A. A., Totzeck, M., Tewes, M., Mincu, R., Khan, M. S., Butler, J., Keller, U., Ahn, J., Bullinger, L., Modest, D. P., Landmesser, U., Lehmann, L. H., Bercker, S., Laufs, U., Böhm, M., Merkely, B., Diek, M., Heise, T., … Rassaf, T. (2025a). Randomized investigation of heart failure therapy in patients with advanced cancer at risk of cardiac wasting: Rationale and design of the EMPATICC trial. *European Journal of Heart Failure*, *27*, 1905–1917. https://doi.org/10.1002/ejhf.3799

Anker, M. S., Mahabadi, A. A., Totzeck, M., Tewes, M., Shahzeb Khan, M., Mincu, R. I., Hendgen-Cotta, U. B., Michel, L., Mathew, B., Drescher, O., Schuler, M., Keller, U., Rieger, K., Ahn, J., Bullinger, L., Modest, D. P., Denecke, C., Kretzler, L., Ramer, L. V., … Rassaf, T. (2025b). Heart failure therapy in patients with advanced cancer receiving specialized palliative care (EMPATICC trial). *European Journal of Heart Failure*, *27*(10), 1905–1917. https://doi.org/10.1002/ejhf.3799

Anker, M. S., Rashid, A. M., Butler, J., & Khan, M. S. (2025). Cardiac wasting in patients with cancer. *Basic Research in Cardiology*, *120*, 25–34. https://doi.org/10.1007/s00395-024-01079-5

Anker, M. S., Rassaf, T., Zamorano, J. L., Khan, M. S., & Landmesser, U. (2024). Cardiac wasting and cancer. *European Heart Journal*, *45*, 3135–3137. https://doi.org/10.1093/eurheartj/ehae438

Anker, M. S., Sanz, A. P., Zamorano, J. L., Mehra, M. R., Butler, J., Riess, H., Coats, A. J. S., & Anker, S. D. (2020). Advanced cancer is also a heart failure syndrome—A hypothesis. *European Journal of Heart Failure 23*(1): 140–144. https://doi.org/10.1002/ejhf.2071

Asnani, A. (2023). New insights into cardiac wasting in patients with cancer*. *JACC*, *81*, 1587–1589. https://doi.org/10.1016/j.jacc.2023.02.035

Asp, M. L., Tian, M., Wendel, A. A., & Belury, M. A. (2010). Evidence for the contribution of insulin resistance to the development of cachexia in tumor-bearing mice. *International Journal of Cancer*, *126*, 756–763. https://doi.org/10.1002/ijc.24784

Ausoni, S., Calamelli, S., Saccà, S., & Azzarello, G. (2020). How progressive cancer endangers the heart: An intriguing and underestimated

problem. *Cancer Metastasis Reviews*, *39*, 535–552. https://doi.org/10.1007/s10555-020-09869-8

Bagnall, L., Grundmann, O., Teolis, M. G., & Yoon, S. L. (2023). Biomarkers and mechanisms associated with cancer-induced cardiac cachexia: A systematic review. *Journal of Cachexia, Sarcopenia and Muscle*, *14*, 1900–1905. https://doi.org/10.1002/jcsm.13267

Balsano, R., Kruize, Z., Lunardi, M., Comandatore, A., Barone, M., Cavazzoni, A., Re Cecconi, A. D., Morelli, L., Wilmink, H., Tiseo, M., Garajovà, I., van Zuylen, L., Giovannetti, E., & Piccirillo, R. (2022). Transforming growth factor-beta signaling in cancer-induced cachexia: From molecular pathways to the clinics. *Cells*, *11*, 2671. https://doi.org/10.3390/cells11172671

Baracos, V. E., Martin, L., Korc, M., Guttridge, D. C., & Fearon, K. C. H. (2018). Cancer-associated cachexia. *Nature Reviews. Disease Primers*, *4*, 17105. https://doi.org/10.1038/nrdp.2017.105

Barkhudaryan, A., Scherbakov, N., Springer, J., & Doehner, W. (2017). Cardiac muscle wasting in individuals with cancer cachexia. *ESC Heart Failure*, *4*, 458–467. https://doi.org/10.1002/ehf2.12184

Belloum, Y., Rannou-Bekono, F., & Favier, F. B. (2017). Cancer-induced cardiac cachexia: Pathogenesis and impact of physical activity (review). *Oncology Reports*, *37*, 2543–2552. https://doi.org/10.3892/or.2017.5542

Beutler, B., & Cerami, A. (1986). Cachectin and tumour necrosis factor as two sides of the same biological coin. *Nature*, *320*, 584–588. https://doi.org/10.1038/320584a0

Bing, C. (2005). Insight into the growth hormone-insulin-like growth factor-I axis in cancer cachexia. *The British Journal of Nutrition*, *93*, 761–763. https://doi.org/10.1079/BJN20051459

Bing, C., Bao, Y., Jenkins, J., Sanders, P., Manieri, M., Cinti, S., Tisdale, M. J., & Trayhurn, P. (2004). Zinc-alpha2-glycoprotein, a lipid mobilizing factor, is expressed in adipocytes and is up-regulated in mice with cancer cachexia. *Proceedings of the National Academy of Sciences of the United States of America*, *101*, 2500–2505.

Buoncervello, M., Maccari, S., Ascione, B., Gambardella, L., Marconi, M., Spada, M., Macchia, D., Stati, T., Patrizio, M., Malorni, W., Matarrese, P., Marano, G., & Gabriele, L. (2019). Inflammatory cytokines associated with cancer growth induce mitochondria and cytoskeleton alterations in cardiomyocytes. *Journal of Cellular Physiology*, *234*, 20453–20468. https://doi.org/10.1002/jcp.28647

Calamelli, S., Noto, S., Baldoni, A., Casarin, A., Calzavara, A., Bolgan, I., Coccato, S., Saccà, S., Laurino, L., Azzarello, G., & Ausoni, S. (2023). Cardiac wasting in head and neck cancer and in cardiac autopsies from different cancer types: A study in a chemo-naïve setting. *Journal of Cachexia, Sarcopenia and Muscle*, *14*, 1286–1298. https://doi.org/10.1002/jcsm.13217

Čelutkienė, J., Pudil, R., López-Fernández, T., Grapsa, J., Nihoyannopoulos, P., Bergler-Klein, J., Cohen-Solal, A., Farmakis, D., Tocchetti, C. G., von Haehling, S., Barberis, V., Flachskampf, F. A., Čeponienė, I., Haegler-Laube, E., Suter, T., Lapinskas, T., Prasad, S., de Boer, R. A., Wechalekar, K., … Lyon, A. R. (2020). Role of cardiovascular imaging in cancer patients receiving cardiotoxic therapies: A position statement on behalf of the Heart Failure Association (HFA), the European Association of Cardiovascular Imaging (EACVI) and the Cardio-Oncology Council of the European Society of Cardiology (ESC). *European Journal of Heart Failure*, *22*, 1504–1524. https://doi.org/10.1002/ejhf.1957

Chen, Y. R., & Zweier, J. L. (2014). Cardiac mitochondria and reactive oxygen species generation. *Circulation Research*, *114*, 524–537. https://doi.org/10.1161/CIRCRESAHA.114.300559

Contaldi, C., D'Aniello, C., Panico, D., Zito, A., Calabrò, P., Di Lorenzo, E., Golino, P., & Montesarchio, V. (2025). Cancer-therapy-related cardiac dysfunction: Latest advances in prevention and treatment. *Life*, *15*, 471. https://doi.org/10.3390/life15030471

Copeland, G. P., Leinster, S. J., Davis, J. C., & Hipkin, L. J. (1987). Insulin resistance in patients with colorectal cancer. *The British Journal of Surgery*, *74*, 1031–1035. https://doi.org/10.1002/bjs.1800741124

Cosper, P. F., & Leinwand, L. A. (2011). Cancer causes cardiac atrophy and autophagy in a sexually dimorphic manner. *Cancer Research*, *71*, 1710–1720. https://doi.org/10.1158/0008-5472.CAN-10-3145

Costelli, P., Carbó, N., Tessitore, L., Bagby, G. J., Lopez-Soriano, F. J., Argilés, J. M., & Baccino, F. M. (1993). Tumor necrosis factor-alpha mediates changes in tissue protein turnover in a rat cancer cachexia model. *The Journal of Clinical Investigation*, *92*, 2783–2789. https://doi.org/10.1172/JCI116897

Courneya, K. S., Vardy, J. L., O'Callaghan, C. J., Gill, S., Friedenreich, C. M., Wong, R. K. S., Dhillon, H. M., Coyle, V., Chua, N. S., Jonker, D. J., Beale, P. J., Haider, K., Tang, P. A., Bonaventura, T., Wong, R., Lim, H. J., Burge, M. E., Hubay, S., Sanatani, M., … Investigators, C. (2025). Structured exercise after adjuvant chemotherapy for colon cancer. *The New England Journal of Medicine*, *393*, 13–25.

Cove-Smith, L., Woodhouse, N., Hargreaves, A., Kirk, J., Smith, S., Price, S. A., Galvin, M., Betts, C. J., Brocklehurst, S., Backen, A., Radford, J., Linton, K., Roberts, R. A., Schmitt, M., Dive, C., Tugwood, J. D., Hockings, P. D., & Mellor, H. R. (2014). An integrated characterization of serological, pathological, and functional events in doxorubicin-induced cardiotoxicity. *Toxicological Sciences*, *140*, 3–15. https://doi.org/10.1093/toxsci/kfu057

Cramer, L., Hildebrandt, B., Kung, T., Wichmann, K., Springer, J., Doehner, W., Sandek, A., Valentova, M., Stojakovic, T., Scharnagl, H., Riess, H., Anker, S. D., & von Haehling, S. (2014). Cardiovascular function and predictors of exercise capacity in patients with colorectal cancer. *Journal of the American College of Cardiology*, *64*, 1310–1319. https://doi.org/10.1016/j.jacc.2014.07.948

Crawford, J., Calle, R. A., Collins, S. M., Weng, Y., Lubaczewski, S. L., Buckeridge, C., Wang, E. Q., Harrington, M. A., Tarachandani, A., Rossulek, M. I., & Revkin, J. H. (2023). Abstract CT108: First-in-patient study of the GDF-15 inhibitor ponsegromab in patients with cancer and cachexia: Safety, tolerability, and exploratory measures of efficacy. *Cancer Research*, *83*:CT108-CT, CT108. https://doi.org/10.1158/1538-7445.AM2023-CT108

Dahlman, I., Mejhert, N., Linder, K., Agustsson, T., Mutch, D. M., Kulyte, A., Isaksson, B., Permert, J., Petrovic, N., Nedergaard, J., Sjölin, E., Brodin, D., Clement, K., Dahlman-Wright, K., Rydén, M., & Arner, P. (2010). Adipose tissue pathways involved in weight loss of cancer cachexia. *British Journal of Cancer*, *102*, 1541–1548. https://doi.org/10.1038/sj.bjc.6605665

Delfinis, L. J., Bellissimo, C. A., Gandhi, S., DiBenedetto, S. N., Garibotti, M. C., Thuhan, A. K., Tsitkanou, S., Rosa-Caldwell, M. E., Rahman, F. A., Cheng, A. J., Wiggs, M. P., Schlattner, U., Quadrilatero, J., Greene, N. P., & Perry, C. G. (2022). Muscle weakness precedes atrophy during cancer cachexia and is linked to muscle-specific mitochondrial stress. *JCI Insight*, *7*, e155147. https://doi.org/10.1172/jci.insight.155147

Ding, H., Zhang, G., Sin, K. W., Liu, Z., Lin, R. K., Li, M., & Li, Y. P. (2017). Activin A induces skeletal muscle catabolism via p38β mitogen-activated protein kinase. *Journal of Cachexia, Sarcopenia and Muscle*, *8*, 202–212. https://doi.org/10.1002/jcsm.12145

Drott, C., Ekman, L., Holm, S., Waldenstrom, A., & Lundholm, K. (1986). Effects of tumor-load and malnutrition on myocardial function in the isolated working rat heart. *Journal of Molecular and Cellular Cardiology*, *18*, 1165–1176. https://doi.org/10.1016/S0022-2828(86)80042-6

Drott, C., & Lundholm, K. (1990). Glucose uptake and amino acid metabolism in perfused hearts from tumor-bearing rats. *The Journal of Surgical Research*, *49*, 62–68. https://doi.org/10.1016/0022-4804(90)90112-F

Dunne, R. F., Crawford, J., Smoyer, K. E., McRae, T. D., Rossulek, M. I., Revkin, J. H., Tarasenko, L. C., & Bonomi, P. D. (2024). The mortality burden of cachexia or weight loss in patients with colorectal or

pancreatic cancer: A systematic literature review. *Journal of Cachexia, Sarcopenia and Muscle*, *15*, 1628–1640. https://doi.org/10.1002/jcsm.13510

Fearon, K., Strasser, F., Anker, S. D., Bosaeus, I., Bruera, E., Fainsinger, R. L., Jatoi, A., Loprinzi, C., MacDonald, N., Mantovani, G., Davis, M., Muscaritoli, M., Ottery, F., Radbruch, L., Ravasco, P., Walsh, D., Wilcock, A., Kaasa, S., & Baracos, V. E. (2011). Definition and classification of cancer cachexia: An international consensus. *The Lancet Oncology*, *12*, 489–495. https://doi.org/10.1016/S1470-2045(10)70218-7

Fröhlich, A. K., Porthun, J., Talha, K. M., Lena, A., Hadzibegovic, S., Wilkenshoff, U., Sonntag, F., Nikolski, A., Ramer, L. V., Zeller, T., Keller, U., Bullinger, L., Anker, S. D., Haverkamp, W., von Haehling, S., Doehner, W., Rauch, U., Skurk, C., Cleland, J. G. F., … Anker, M. S. (2024). Association of an impaired GH-IGF-I axis with cardiac wasting in patients with advanced cancer. *Clinical Research in Cardiology*, *114*, 1118–1132. https://doi.org/10.1007/s00392-024-02400-x

Garcia-Garduño, T. C., Padilla-Gutierrez, J. R., Cambrón-Mora, D., & Valle, Y. (2021). RAAS: A convergent player in ischemic heart failure and cancer. *International Journal of Molecular Sciences*, *22*, 7106. https://doi.org/10.3390/ijms22137106

Gunadi, J. W., Welliangan, A. S., Soetadji, R. S., Jasaputra, D. K., & Lesmana, R. (2021). The role of autophagy modulated by exercise in cancer cachexia. *Life (Basel)*, *11*, 781. https://doi.org/10.3390/life11080781

Hadzibegovic, S., Porthun, J., Lena, A., Weinländer, P., Lück, L. C., Potthoff, S. K., Rösnick, L., Fröhlich, A. K., Ramer, L. V., Sonntag, F., Wilkenshoff, U., Ahn, J., Keller, U., Bullinger, L., Mahabadi, A. A., Totzeck, M., Rassaf, T., von Haehling, S., Coats, A. J. S., … Anker, M. S. (2023). Hand grip strength in patients with advanced cancer: A prospective study. *Journal of Cachexia, Sarcopenia and Muscle*, *14*, 1682–1694. https://doi.org/10.1002/jcsm.13248

Heckmann, M. B., Totakhel, B., Finke, D., Anker, M. S., Muller-Tidow, C., Haberkorn, U., Katus, H. A., & Lehmann, L. H. (2019). Evidence for a cardiac metabolic switch in patients with Hodgkin's lymphoma. *ESC Heart Failure*, *6*, 824–829. https://doi.org/10.1002/ehf2.12475

Hinch, E. C., Sullivan-Gunn, M. J., Vaughan, V. C., McGlynn, M. A., & Lewandowski, P. A. (2013). Disruption of pro-oxidant and antioxidant systems with elevated expression of the ubiquitin proteosome system in the cachectic heart muscle of nude mice. *Journal of Cachexia, Sarcopenia and Muscle*, *4*, 287–293. https://doi.org/10.1007/s13539-013-0116-8

Hosny, N., Cohen, H., Elafany, M. W., Schreifels, J., Bauer, J., Gulati, R., Thompson, B. R., Liu, J. C., & Metzger, J. M. (2025). Elucidating cancer cachexia-mediated aberrant cardiac wasting signaling in human iPSC-derived cardiac muscle. *bioRxiv*, 2025.08.18.670675. https://doi.org/10.1101/2025.08.18.670675

Iaia, N., Noviello, C., Muscaritoli, M., & Costelli, P. (2025). Inflammation in cancer cachexia: Still the central tenet or just another player? *American Journal of Physiology-Cell Physiology*, *328*, C1837–C1852. https://doi.org/10.1152/ajpcell.00808.2024

Ioffe, D., Bhatia-Patel, S. C., Gandhi, S., Hamad, E. A., & Dotan, E. (2024). Cardiovascular concerns, cancer treatment, and biological and chronological aging in cancer: JACC family series. *JACC. CardioOncology*, *6*, 143–158. https://doi.org/10.1016/j.jaccao.2024.02.001

Ishida, J., Saitoh, M., Doehner, W., von Haehling, S., Anker, M., Anker, S. D., & Springer, J. (2017). Animal models of cachexia and sarcopenia in chronic illness: Cardiac function, body composition changes and therapeutic results. *International Journal of Cardiology*, *238*, 12–18. https://doi.org/10.1016/j.ijcard.2017.03.154

Karlstaedt, A., Barrett, M., Hu, R., Gammons, S. T., & Ky, B. (2021). Cardio-oncology: Understanding the intersections between cardiac metabolism and cancer biology. *JACC: Basic to Translational Science*, *6*, 705–718. https://doi.org/10.1016/j.jacbts.2021.05.008

Karlstaedt, A., Moslehi, J., & de Boer, R. A. (2022). Cardio-onco-metabolism: Metabolic remodelling in cardiovascular disease and cancer. *Nature Reviews. Cardiology*, *19*, 414–425. https://doi.org/10.1038/s41569-022-00698-6

Karlstaedt, A., Zhang, X., Vitrac, H., Harmancey, R., Vasquez, H., Wang, J. H., Goodell, M. A., & Taegtmeyer, H. (2016). Oncometabolite D-2-hydroxyglutarate impairs alpha-ketoglutarate dehydrogenase and contractile function in rodent heart. *Proceedings of the National Academy of Sciences of the United States of America*, *113*, 10436–10441.

Kazemi-Bajestani, S. M. R., Becher, H., Butts, C., Basappa, N. S., Smylie, M., Joy, A. A., Sangha, R., Gallivan, A., Kavsak, P., Chu, Q., & Baracos, V. E. (2019). Rapid atrophy of cardiac left ventricular mass in patients with non-small cell carcinoma of the lung. *Journal of Cachexia, Sarcopenia and Muscle*, *10*, 1070–1082. https://doi.org/10.1002/jcsm.12451

Law, M. L., & Metzger, J. M. (2021). Cardiac myocyte intrinsic contractility and calcium handling deficits underlie heart organ dysfunction in murine cancer cachexia. *Scientific Reports*, *11*, 23627. https://doi.org/10.1038/s41598-021-02688-z

Lee, D. E., Brown, J. L., Rosa-Caldwell, M. E., Perry, R. A., Brown, L. A., Haynie, W. S., Washington, T. A., Wiggs, M. P., Rajaram, N., & Greene, N. P. (2021). Cancer-induced cardiac atrophy adversely affects myocardial redox state and mitochondrial oxidative characteristics. *JCSM Rapid Communications*, *4*, 3–15. https://doi.org/10.1002/rco2.18

Lena, A., Coats, A. J. S., & Anker, M. S. (2018). Metabolic disorders in heart failure and cancer. *ESC Heart Failure*, *5*, 1092–1098. https://doi.org/10.1002/ehf2.12389

Lena, A., Ebner, N., & Anker, M. S. (2019). Cardiac cachexia. *European Heart Journal Supplements*, *21*, L24–L27. https://doi.org/10.1093/eurheartj/suz241

Lena, A., Ebner, N., Coats, A. J. S., & Anker, M. S. (2019). Cardiac cachexia: The mandate to increase clinician awareness. *Current Opinion in Supportive and Palliative Care*, *13*, 298–304. https://doi.org/10.1097/SPC.0000000000000456

Lena, A., Hadzibegovic, S., von Haehling, S., Springer, J., Coats, A. J., & Anker, M. S. (2021). Sarcopenia and cachexia in chronic diseases: From mechanisms to treatment. *Polish Archives of Internal Medicine*, *131*, 16135. https://doi.org/10.20452/pamw.16135

Lena, A., Wilkenshoff, U., Hadzibegovic, S., Porthun, J., Rosnick, L., Frohlich, A. K., Zeller, T., Karakas, M., Keller, U., Ahn, J., Bullinger, L., Riess, H., Rosen, S. D., Lyon, A. R., Luscher, T. F., Totzeck, M., Rassaf, T., Burkhoff, D., Mehra, M. R., … Anker, M. S. (2023). Clinical and prognostic relevance of cardiac wasting in patients with advanced cancer. *Journal of the American College of Cardiology*, *81*, 1569–1586. https://doi.org/10.1016/j.jacc.2023.02.039

Lopaschuk, G. D., Karwi, Q. G., Tian, R., Wende, A. R., & Abel, E. D. (2021). Cardiac energy metabolism in heart failure. *Circulation Research*, *128*, 1487–1513. https://doi.org/10.1161/CIRCRESAHA.121.318241

Lyon, A. R., Dent, S., Stanway, S., Earl, H., Brezden-Masley, C., Cohen-Solal, A., Tocchetti, C. G., Moslehi, J. J., Groarke, J. D., Bergler-Klein, J., Khoo, V., Tan, L. L., Anker, M. S., von Haehling, S., Maack, C., Pudil, R., Barac, A., Thavendiranathan, P., Ky, B., … Lenihan, D. (2020). Baseline cardiovascular risk assessment in cancer patients scheduled to receive cardiotoxic cancer therapies: A position statement and new risk assessment tools from the Cardio-Oncology Study Group of the Heart Failure Association of the European Society of Cardiology in collaboration with the International Cardio-Oncology Society. *European Journal of Heart Failure*, *22*, 1945–1960. https://doi.org/10.1002/ejhf.1920

Manne, N. D., Lima, M., Enos, R. T., Wehner, P., Carson, J. A., & Blough, E. (2013). Altered cardiac muscle mTOR regulation during the progression of cancer cachexia in the ApcMin/+ mouse. *International Journal of Oncology*, *42*, 2134–2140. https://doi.org/10.3892/ijo.2013.1893

Mariean, C. R., Tiucă, O. M., Mariean, A., & Cotoi, O. S. (2023). Cancer cachexia: New insights and future directions. *Cancers (Basel)*, *15*, 5590. https://doi.org/10.3390/cancers15235590

Matsuyama, T., Ishikawa, T., Okayama, T., Oka, K., Adachi, S., Mizushima, K., Kimura, R., Okajima, M., Sakai, H., Sakamoto, N., Katada, K., Kamada, K., Uchiyama, K., Handa, O., Takagi, T., Kokura, S., Naito, Y., & Itoh, Y. (2015). Tumor inoculation site affects the development of cancer cachexia and muscle wasting. *International Journal of Cancer*, *137*, 2558–2565. https://doi.org/10.1002/ijc.29620

Moulin, M., Piquereau, J., Mateo, P., Fortin, D., Rucker-Martin, C., Gressette, M., Lefebvre, F., Gresikova, M., Solgadi, A., Veksler, V., Garnier, A., & Ventura-Clapier, R. (2015). Sexual dimorphism of doxorubicin-mediated cardiotoxicity: Potential role of energy metabolism remodeling. *Circulation. Heart Failure*, *8*, 98–108. https://doi.org/10.1161/CIRCHEARTFAILURE.114.001180

Mulder, F. I., Horváth-Puhó, E., van Es, N., Pedersen, L., Büller, H. R., Cronin-Fenton, D., Christiansen, C. F., Bøtker, H. E., Bhaskaran, K., & Sørensen, H. T. (2025). Risk of cardiovascular disease in cancer survivors after systemic treatment: A population-based cohort study. *JACC: CardioOncology*, *7*, 360–378. https://doi.org/10.1016/j.jaccao.2025.03.008

Musolino, V., Palus, S., Tschirner, A., Drescher, C., Gliozzi, M., Carresi, C., Vitale, C., Muscoli, C., Doehner, W., von Haehling, S., Anker, S. D., Mollace, V., & Springer, J. (2016). Megestrol acetate improves cardiac function in a model of cancer cachexia-induced cardiomyopathy by autophagic modulation. *Journal of Cachexia, Sarcopenia and Muscle*, *7*, 555–566. https://doi.org/10.1002/jcsm.12116

Ogilvie, L. M., Delfinis, L. J., Coyle-Asbil, B., Vudatha, V., Alshamali, R., Garlisi, B., Pereira, M., Matuszewska, K., Garibotti, M. C., Gandhi, S., Brunt, K. R., Wood, G. A., Trevino, J. G., Perry, C. G. R., Petrik, J., & Simpson, J. A. (2024). Cardiac atrophy, dysfunction, and metabolic impairments: A cancer-induced cardiomyopathy phenotype. *The American Journal of Pathology*, *194*, 1823–1843. https://doi.org/10.1016/j.ajpath.2024.06.008

Palus, S., von Haehling, S., Flach, V. C., Tschirner, A., Doehner, W., Anker, S. D., & Springer, J. (2013). Simvastatin reduces wasting and improves cardiac function as well as outcome in experimental cancer cachexia. *International Journal of Cardiology*, *168*, 3412–3418. https://doi.org/10.1016/j.ijcard.2013.04.150

Parry, T. L., & Hayward, R. (2018). Exercise protects against cancer-induced cardiac cachexia. *Medicine and Science in Sports and Exercise*, *50*, 1169–1176. https://doi.org/10.1249/MSS.0000000000001544

Parry, T. L., Tichy, L., & Brantley, J. T. (2022). Cardioprotective effects of preconditioning exercise in the female tumor bearing mouse. *Frontiers in Cell and Development Biology*, *10*, 950479. https://doi.org/10.3389/fcell.2022.950479

Pietzsch, S., Ricke-Hoch, M., Stapel, B., & Hilfiker-Kleiner, D. (2020). Modulation of cardiac AKT and STAT3 signalling in preclinical cancer models and their impact on the heart. *Biochimica et Biophysica Acta, Molecular Cell Research*, *1867*, 118519. https://doi.org/10.1016/j.bbamcr.2019.07.014

Pudil, R., Mueller, C., Čelutkienė, J., Henriksen, P. A., Lenihan, D., Dent, S., Barac, A., Stanway, S., Moslehi, J., Suter, T. M., Ky, B., Štěrba, M., Cardinale, D., Cohen-Solal, A., Tocchetti, C. G., Farmakis, D., Bergler-Klein, J., Anker, M. S., Von Haehling, S., … Lyon, A. R. (2020). Role of serum biomarkers in cancer patients receiving cardiotoxic cancer therapies: A position statement from the Cardio-Oncology Study Group of the Heart Failure Association and the Cardio-Oncology Council of the European Society of Cardiology. *European Journal of Heart Failure*, *22*, 1966–1983. https://doi.org/10.1002/ejhf.2017

Raun, S. H., Knudsen, J. R., Han, X., Jensen, T. E., & Sylow, L. (2022). Cancer causes dysfunctional insulin signaling and glucose transport in a muscle-type-specific manner. *The FASEB Journal*, *36*, e22211. https://doi.org/10.1096/fj.202101759R

Rupert, J. E., Narasimhan, A., Jengelley, D. H. A., Jiang, Y., Liu, J., Au, E., Silverman, L. M., Sandusky, G., Bonetto, A., Cao, S., Lu, X., O'Connell, T. M., Liu, Y., Koniaris, L. G., & Zimmers, T. A. (2021). Tumor-derived IL-6 and trans-signaling among tumor, fat, and muscle mediate pancreatic cancer cachexia. *The Journal of Experimental Medicine*, *218*, e20190450. https://doi.org/10.1084/jem.20190450

Saha, S., Singh, P. K., Roy, P., & Kakar, S. S. (2022). Cardiac cachexia: Unaddressed aspect in cancer patients. *Cells*, *11*, 990. https://doi.org/10.3390/cells11060990

Sandri, M. (2016). Protein breakdown in cancer cachexia. *Seminars in Cell & Developmental Biology*, *54*, 11–19. https://doi.org/10.1016/j.semcdb.2015.11.002

Schafer, M., Oeing, C. U., Rohm, M., Baysal-Temel, E., Lehmann, L. H., Bauer, R., Volz, H. C., Boutros, M., Sohn, D., Sticht, C., Gretz, N., Eichelbaum, K., Werner, T., Hirt, M. N., Eschenhagen, T., Muller-Decker, K., Strobel, O., Hackert, T., Krijgsveld, J., … Herzig, S. (2016). Ataxin-10 is part of a cachexokine cocktail triggering cardiac metabolic dysfunction in cancer cachexia. *Molecular Metabolism*, *5*, 67–78. https://doi.org/10.1016/j.molmet.2015.11.004

Setiawan, T., Sari, I. N., Wijaya, Y. T., Julianto, N. M., Muhammad, J. A., Lee, H., Chae, J. H., & Kwon, H. Y. (2023). Cancer cachexia: Molecular mechanisms and treatment strategies. *Journal of Hematology & Oncology*, *16*, 54. https://doi.org/10.1186/s13045-023-01454-0

Springer, J., Palus, S., Rauchhaus, M., & Anker, S. D. (2008). Experimental cancer cachexia severely impairs heart function. *Journal of Cardiac Failure*, *14*, S18. https://doi.org/10.1016/j.cardfail.2008.06.063

Springer, J., Tschirner, A., Haghikia, A., von Haehling, S., Lal, H., Grzesiak, A., Kaschina, E., Palus, S., Potsch, M., von Websky, K., Hocher, B., Latouche, C., Jaisser, F., Morawietz, L., Coats, A. J., Beadle, J., Argiles, J. M., Thum, T., Foldes, G., … Anker, S. D. (2014). Prevention of liver cancer cachexia-induced cardiac wasting and heart failure. *European Heart Journal*, *35*, 932–941. https://doi.org/10.1093/eurheartj/eht302

Stevens, S. C. W., Velten, M., Youtz, D. J., Clark, Y., Jing, R., Reiser, P. J., Bicer, S., Devine, R. D., McCarthy, D. O., & Wold, L. E. (2015). Losartan treatment attenuates tumor-induced myocardial dysfunction. *Journal of Molecular and Cellular Cardiology*, *85*, 37–47. https://doi.org/10.1016/j.yjmcc.2015.05.007

Sturgeon, K. M., Deng, L., Bluethmann, S. M., Zhou, S., Trifiletti, D. M., Jiang, C., Kelly, S. P., & Zaorsky, N. G. (2019). A population-based study of cardiovascular disease mortality risk in US cancer patients. *European Heart Journal*, *40*, 3889–3897. https://doi.org/10.1093/eurheartj/ehz766

Tanaka, T., Kanda, T., Takahashi, T., Saegusa, S., Moriya, J., & Kurabayashi, M. (2004). Interleukin-6-induced reciprocal expression of SERCA and natriuretic peptides mRNA in cultured rat ventricular myocytes. *The Journal of International Medical Research*, *32*, 57–61. https://doi.org/10.1177/147323000403200109

Thackeray, J. T., Pietzsch, S., Stapel, B., Ricke-Hoch, M., Lee, C. W., Bankstahl, J. P., Scherr, M., Heineke, J., Scharf, G., Haghikia, A., Bengel, F. M., & Hilfiker-Kleiner, D. (2017). Insulin supplementation attenuates cancer-induced cardiomyopathy and slows tumor disease progression. *JCI Insight*, *2*, e93098. https://doi.org/10.1172/jci.insight.93098

Tian, M., Asp, M. L., Nishijima, Y., & Belury, M. A. (2011). Evidence for cardiac atrophic remodeling in cancer-induced cachexia in mice. *International Journal of Oncology*, *39*, 1321–1326. https://doi.org/10.3892/ijo.2011.1150

Tian, M., Nishijima, Y., Asp, M. L., Stout, M. B., Reiser, P. J., & Belury, M. A. (2010). Cardiac alterations in cancer-induced cachexia in mice. *International Journal of Oncology*, *37*, 347–353. https://doi.org/10.3892/ijo_00000683

Tichy, L., Allred, K. F., Rezeli, E. T., Coleman, M. F., Allred, C. D., Hursting, S. D., & Parry, T. L. (2025). Concurrent physical activity protects against C26 adenocarcinoma tumor-mediated cardiac and skeletal muscle dysfunction and wasting in males. *Cells*, *14*, 924. https://doi.org/10.3390/cells14120924

Tichy, L., & Parry, T. L. (2023). The pathophysiology of cancer-mediated cardiac cachexia and novel treatment strategies: A narrative review. *Cancer Medicine*, *12*, 17706–17717.

Toledo, M., Busquets, S., Penna, F., Zhou, X., Marmonti, E., Betancourt, A., Massa, D., López-Soriano, F. J., Han, H. Q., & Argilés, J. M. (2016). Complete reversal of muscle wasting in experimental cancer cachexia: Additive effects of activin type II receptor inhibition and β-2 agonist. *International Journal of Cancer*, *138*, 2021–2029. https://doi.org/10.1002/ijc.29930

Trobec, K., Palus, S., Tschirner, A., von Haehling, S., Doehner, W., Lainscak, M., Anker, S. D., & Springer, J. (2014). Rosiglitazone reduces body wasting and improves survival in a rat model of cancer cachexia. *Nutrition*, *30*, 1069–1075. https://doi.org/10.1016/j.nut.2013.12.005

Trobec, K., von Haehling, S., Anker, S. D., & Lainscak, M. (2011). Growth hormone, insulin-like growth factor 1, and insulin signaling—A pharmacological target in body wasting and cachexia. *Journal of Cachexia, Sarcopenia and Muscle*, *2*, 191–200. https://doi.org/10.1007/s13539-011-0043-5

von Haehling, S., Doehner, W., & Anker, S. D. (2007). Nutrition, metabolism, and the complex pathophysiology of cachexia in chronic heart failure. *Cardiovascular Research*, *73*, 298–309. https://doi.org/10.1016/j.cardiores.2006.08.018

Vonk-Noordegraaf, A. (2010). The shrinking heart in chronic obstructive pulmonary disease. *The New England Journal of Medicine*, *362*, 267–268.

Vudatha, V., Devarakonda, T., Liu, C., Freudenberger, D. C., Riner, A. N., Herremans, K. M., & Trevino, J. G. (2022). Review of mechanisms and treatment of cancer-induced cardiac cachexia. *Cells*, *11*(6), 1040. https://doi.org/10.3390/cells11061040

Wang, Y. P., Zhang, R. Q., Li, N., Wang, Q. S., Yu, K., Fan, M., Zhang, X. W., Feng, L. X., & Liu, X. (2024). The involvement and possible targeting of cardiolipins degradation and disturbed linoleic acid metabolism in cardiac atrophy under cancer cachexia. *European Journal of Pharmacology*, *985*, 177108. https://doi.org/10.1016/j.ejphar.2024.177108

Wisneski, J. A., Gertz, E. W., Neese, R. A., & Mayr, M. (1987). Myocardial metabolism of free fatty acids. Studies with 14C-labeled substrates in humans. *The Journal of Clinical Investigation*, *79*, 359–366.

Wysong, A., Couch, M., Shadfar, S., Li, L., Rodriguez, J. E., Asher, S., Yin, X., Gore, M., Baldwin, A., Patterson, C., & Willis, M. S. (2011). NF-κB inhibition protects against tumor-induced cardiac atrophy in vivo. *The American Journal of Pathology*, *178*, 1059–1068. https://doi.org/10.1016/j.ajpath.2010.12.009

Yu, J., Leibiger, B., Yang, S. N., Shears, S. B., Leibiger, I. B., Berggren, P. O., & Barker, C. J. (2023). Multiple inositol polyphosphate phosphatase compartmentalization separates inositol phosphate metabolism from inositol lipid signaling. *Biomolecules*, *13*(6), 885. https://doi.org/10.3390/biom13060885

Zhou, X., Wang, J. L., Lu, J., Song, Y., Kwak, K. S., Jiao, Q., Rosenfeld, R., Chen, Q., Boone, T., Simonet, W. S., Lacey, D. L., Goldberg, A. L., & Han, H. Q. (2010). Reversal of cancer cachexia and muscle wasting by ActRIIB antagonism leads to prolonged survival. *Cell*, *142*, 531–543.

How to cite this article: Lena, A., Khan, M. S., Keller, U., Bullinger, L., Modest, D. P., & Anker, M. S. (2026). A comprehensive review of cancer-induced cardiac wasting. *British Journal of Pharmacology*, 1–14. https://doi.org/10.1111/bph.70461