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# PHARMACOLOGICAL PREVENTION OF CHEMOTHERAPY-INDUCED CARDIOTOXICITY: COMPARATIVE EVIDENCE ON BETA-BLOCKERS AND ACE INHIBITORS IN ONCOLOGY

# PREVENÇÃO FARMACOLÓGICA DA CARDIOTOXICIDADE INDUZIDA POR QUIMIOTERAPIA: EVIDÊNCIAS COMPARATIVAS ENTRE BETABLOQUEADORES E INIBIDORES DA ECA EM ONCOLOGIA

# PREVENCIÓN FARMACOLÓGICA DE LA CARDIOTOXICIDAD INDUCIDA POR QUIMIOTERAPIA: EVIDENCIA COMPARATIVA SOBRE BETABLOQUEANTES E INHIBIDORES DE LA ECA EN ONCOLOGÍA

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## ABSTRACT

**Introduction:** Chemotherapy remains one of the most effective strategies for cancer treatment but frequently results in cardiac dysfunction, particularly in patients exposed to anthracyclines or targeted agents with cardiotoxic potential. Preventive pharmacotherapy with beta-blockers and angiotensin-converting enzyme (ACE) inhibitors has emerged as a viable approach to preserving myocardial function in this population.

**Objective:** To analyze the comparative efficacy of beta-blockers and ACE inhibitors, individually and in combination, in the prevention of chemotherapy-induced cardiotoxicity in cancer patients at high cardiovascular risk. Secondary objectives included assessment of safety, tolerability, and long-term effects on cardiac remodeling.

**Methods:** A systematic literature review was conducted in PubMed, Scopus, Web of Science, Cochrane Library, ClinicalTrials.gov, and LILACS. Studies published between 2015 and 2025 were included. Randomized controlled trials, cohort studies, and meta-analyses addressing preventive cardioprotective pharmacotherapy were selected.

**Results and Discussion:** Across 30 eligible studies, beta-blockers such as carvedilol and bisoprolol, as well as ACE inhibitors including enalapril and lisinopril, significantly reduced the incidence of left ventricular ejection fraction decline and biomarker elevation. Combination therapy provided synergistic protection and reduced chemotherapy discontinuation due to cardiac dysfunction. Preventive regimens demonstrated excellent safety and tolerability profiles.

**Conclusion:** Beta-blockers and ACE inhibitors constitute effective and safe pharmacological strategies for the prevention of chemotherapy-induced cardiotoxicity. Their routine inclusion

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in cardio-oncology protocols may improve cardiac outcomes, treatment continuity, and overall survivorship.

**Keywords:** Cardiotoxicity. Beta-Blockers. ACE Inhibitors. Cardio-Oncology.

## RESUMO

**Introdução:** A quimioterapia continua sendo uma das estratégias mais eficazes para o tratamento do câncer, mas frequentemente resulta em disfunção cardíaca, particularmente em pacientes expostos a antraciclinas ou agentes direcionados com potencial cardiotóxico. A farmacoterapia preventiva com betabloqueadores e inibidores da enzima conversora de angiotensina (ECA) surgiu como uma abordagem viável para preservar a função miocárdica nessa população.

**Objetivo:** Analisar a eficácia comparativa de betabloqueadores e inibidores da ECA, individualmente e em combinação, na prevenção da cardiotoxicidade induzida por quimioterapia em pacientes com câncer de alto risco cardiovascular. Os objetivos secundários incluíram a avaliação da segurança, tolerabilidade e efeitos a longo prazo na remodelação cardíaca.

**Métodos:** Uma revisão sistemática da literatura foi realizada nas bases de dados PubMed, Scopus, Web of Science, Biblioteca Cochrane, ClinicalTrials.gov e LILACS. Estudos publicados entre 2015 e 2025 foram incluídos. Foram selecionados ensaios clínicos randomizados, estudos de coorte e meta-análises que abordassem farmacoterapia cardioprotetora preventiva.

**Resultados e Discussão:** Em 30 estudos elegíveis, betabloqueadores como carvedilol e bisoprolol, bem como inibidores da ECA, incluindo enalapril e lisinopril, reduziram significativamente a incidência de declínio da fração de ejeção do ventrículo esquerdo e elevação de biomarcadores. A terapia combinada proporcionou proteção sinérgica e reduziu a descontinuação da quimioterapia devido à disfunção cardíaca. Os regimes preventivos demonstraram excelentes perfis de segurança e tolerabilidade.

**Conclusão:** Betabloqueadores e inibidores da ECA constituem estratégias farmacológicas eficazes e seguras para a prevenção da cardiotoxicidade induzida por quimioterapia. Sua inclusão rotineira em protocolos de cardio-oncologia pode melhorar os desfechos cardíacos, a continuidade do tratamento e a sobrevida geral.

**Palavras-chave:** Cardiotoxicidade. Betabloqueadores. Inibidores da ECA. Cardio-Oncologia.

## RESUMEN

**Introducción:** La quimioterapia sigue siendo una de las estrategias más eficaces para el tratamiento del cáncer, pero con frecuencia provoca disfunción cardíaca, especialmente en pacientes expuestos a antraciclinas o fármacos dirigidos con potencial cardiotóxico. La farmacoterapia preventiva con betabloqueantes e inhibidores de la enzima convertidora de angiotensina (IECA) se ha convertido en un enfoque viable para preservar la función miocárdica en esta población.

**Objetivo:** Analizar la eficacia comparativa de los betabloqueantes y los IECA, individualmente y en combinación, en la prevención de la cardiotoxicidad inducida por quimioterapia en pacientes con cáncer y alto riesgo cardiovascular. Los objetivos secundarios incluyeron la evaluación de la seguridad, la tolerabilidad y los efectos a largo plazo sobre el remodelado cardíaco.

**Métodos:** Se realizó una revisión sistemática de la literatura en PubMed, Scopus, Web of Science, Cochrane Library, ClinicalTrials.gov y LILACS. Se incluyeron estudios publicados entre 2015 y 2025. Se seleccionaron ensayos controlados aleatorizados, estudios de cohorte y metanálisis que abordaron la farmacoterapia cardioprotectora preventiva.

**Resultados y discusión:** En 30 estudios elegibles, los betabloqueantes, como el carvedilol y el bisoprolol, así como los inhibidores de la ECA, como enalapril y lisinopril, redujeron significativamente la incidencia de disminución de la fracción de eyección del ventrículo izquierdo y la elevación de biomarcadores. La terapia combinada proporcionó protección sinérgica y redujo la interrupción de la quimioterapia debido a disfunción cardíaca. Los regímenes preventivos demostraron excelentes perfiles de seguridad y tolerabilidad.

**Conclusión:** Los betabloqueantes y los inhibidores de la ECA constituyen estrategias farmacológicas eficaces y seguras para la prevención de la cardiotoxicidad inducida por quimioterapia. Su inclusión sistemática en los protocolos de cardiooncología puede mejorar los resultados cardíacos, la continuidad del tratamiento y la supervivencia general.

**Palabras clave:** Cardiotoxicidad. Betabloqueantes. Inhibidores de la ECA. Cardiooncología.

## 1 INTRODUCTION

Chemotherapy-induced cardiotoxicity remains a major concern in modern oncology, representing one of the most frequent and clinically relevant non-hematologic complications of cancer treatment. Among chemotherapeutic agents, anthracyclines are particularly known for their dose-dependent potential to induce left ventricular (LV) dysfunction and heart failure, affecting up to one-third of high-risk patients. Other cardiotoxic drugs, such as HER2-targeted therapies, alkylating agents, and immune checkpoint inhibitors, may further amplify cardiovascular risk. This growing burden of cardiotoxicity has given rise to cardio-oncology, a multidisciplinary field focused on the early detection, prevention, and management of treatment-related cardiovascular adverse effects.

The pathophysiology of anthracycline-induced cardiotoxicity is multifactorial. Experimental studies have demonstrated that oxidative stress, mitochondrial dysfunction, and the inhibition of topoisomerase IIβ are central to the development of myocyte apoptosis and contractile dysfunction. These mechanisms collectively lead to cumulative myocardial injury, manifesting as subclinical LV impairment that may progress to symptomatic heart failure. The risk is heightened in patients with pre-existing hypertension, diabetes, coronary artery disease, or exposure to mediastinal radiation. Hence, preventive interventions are paramount to preserve cardiac function without compromising oncological efficacy.

Beta-blockers have emerged as cornerstone agents in cardioprotection due to their ability to mitigate sympathetic activation and reduce oxidative stress. Among them, carvedilol, a non-selective beta- and alpha-adrenergic blocker, possesses additional antioxidant and anti-apoptotic properties that distinguish it from other agents in its class. Clinical trials have shown that carvedilol attenuates troponin elevation, preserves global longitudinal strain, and limits LV ejection fraction decline during anthracycline therapy. These findings support its preventive use even in asymptomatic patients, making it a preferred option in many cardio-oncology protocols.

Similarly, angiotensin-converting enzyme (ACE) inhibitors such as enalapril play a complementary role in cardioprotection by attenuating neurohormonal activation and improving ventricular remodeling. By blocking the renin–angiotensin–aldosterone system, ACE inhibitors reduce afterload, enhance endothelial function, and prevent maladaptive myocardial fibrosis. Prospective studies have demonstrated that enalapril administration, either prophylactically or triggered by early troponin rise, prevents or reverses subclinical LV dysfunction. The combination of ACE inhibitors with beta-blockers is hypothesized to provide synergistic benefits through the simultaneous modulation of hemodynamic and molecular pathways.

Randomized controlled trials and meta-analyses over the past decade have consolidated the evidence supporting pharmacological cardioprotection in oncology. The OVERCOME trial and subsequent multicenter studies confirmed that carvedilol and enalapril, alone or in combination, reduce the incidence of chemotherapy-related LV dysfunction and cardiac biomarker elevation. Biomarker-guided initiation strategies, using troponin or natriuretic peptide levels to trigger prophylactic therapy, have shown particular promise for individualized care. This approach allows clinicians to target interventions to those at highest risk while avoiding unnecessary exposure in low-risk patients.

Despite these advances, heterogeneity persists across studies regarding optimal timing, dosage, and patient selection. Some trials demonstrate robust benefits, whereas others reveal only modest improvements, reflecting differences in design, population, and chemotherapy regimens. Moreover, long-term data on survival and cardiac recovery remain limited, emphasizing the need for well-powered multicenter trials. Nonetheless, the overall evidence base supports the proactive use of cardioprotective agents in high-risk patients undergoing potentially cardiotoxic chemotherapy.

The safety and tolerability of carvedilol and enalapril have been consistently favorable in the oncology setting. Adverse effects such as mild hypotension, fatigue, or transient changes in renal function are generally well managed and seldom require treatment discontinuation. Importantly, these agents do not interfere with the pharmacokinetics or therapeutic efficacy of anticancer drugs, making them suitable for concurrent use during active chemotherapy.

In summary, pharmacological cardioprotection with beta-blockers and ACE inhibitors represents a practical and evidence-based strategy to reduce chemotherapy-induced cardiotoxicity. Their combined administration offers a path toward integrated cardio-oncological care, aligning the goals of cancer control and cardiovascular preservation. The present review aims to synthesize recent evidence comparing these two classes of agents, individually and in combination, in the prevention of cardiotoxicity among high-risk cancer patients, while discussing safety profiles, biomarker-guided protocols, and implications for clinical practice.

## 2 OBJECTIVES

The primary objective of this review is to evaluate the efficacy of beta-blockers and angiotensin-converting enzyme (ACE) inhibitors—individually and in combination—in the prevention of chemotherapy-induced cardiotoxicity among high-risk oncology patients.

Secondary objectives include:

1. Comparing the effects of each pharmacological class on the preservation of left ventricular ejection fraction (LVEF) and reduction of cardiac biomarkers, such as troponin and NT-proBNP.
2. Assessing the safety and tolerability of these agents during active cancer treatment.
3. Exploring the role of biomarker-guided therapy in optimizing the timing of cardioprotective intervention.
4. Analyzing evidence on long-term outcomes, including the incidence of heart failure, hospitalization, and treatment discontinuation.
5. Identifying research gaps and proposing future directions for clinical trials focused on pharmacological cardioprotection in oncology.

## 3 METHODOLOGY

A comprehensive systematic review was conducted following the PRISMA 2020 (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines to ensure methodological transparency and reproducibility.

### 3.1 SEARCH STRATEGY

Electronic searches were performed in the databases PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov, and the International Clinical Trials Registry Platform (ICTRP). Searches were limited to studies published between January 2015 and March 2025.

The search strategy combined Medical Subject Headings (MeSH) and free-text terms, including:

("chemotherapy-induced cardiotoxicity" OR "anthracycline cardiotoxicity") AND ("beta-blocker" OR "carvedilol" OR "bisoprolol") AND ("ACE inhibitor" OR "enalapril" OR "lisinopril") AND ("cardioprotection" OR "cardio-oncology" OR "prevention").

### 3.2 DATA SYNTHESIS

Given the heterogeneity among study designs and outcome measures, a narrative synthesis was conducted. The findings were summarized qualitatively by pharmacological class, highlighting comparative efficacy, combination strategies, and clinical implementation in cardio-oncology. Where applicable, results from meta-analyses were discussed to strengthen interpretative validity.

### 3.3 ETHICAL CONSIDERATIONS

As this review exclusively analyzed data from previously published studies, no ethical approval or patient consent was required. All included research adhered to the ethical standards of the original institutions and conformed to the Declaration of Helsinki.

## 4 RESULTS

A total of 132 articles were assessed in full, of which 30 studies met the inclusion criteria. These included 16 randomized controlled trials (RCTs), 8 prospective cohort studies, and 6 systematic reviews or meta-analyses. Additionally, a small number of preclinical investigations were reviewed separately for mechanistic insight but were not included in the main synthesis.

The selected studies evaluated beta-blockers (mainly carvedilol and bisoprolol), ACE inhibitors (principally enalapril and lisinopril), and combination regimens. Most participants were adults with breast cancer, lymphoma, or leukemia receiving anthracycline-based chemotherapy, with several trials extending to patients treated with trastuzumab or taxanes. The main outcomes analyzed included left ventricular ejection fraction (LVEF), troponin and NT-proBNP levels, and incidence of symptomatic heart failure or cardiac hospitalization.

The table below summarizes the key findings of the included studies, arranged chronologically by publication year.

**Table 1**

*Main studies evaluating beta-blockers and ACE inhibitors for prevention of chemotherapy-induced cardiotoxicity (2015–2025)*

| Author / Year | Study Type / Intervention | Main Outcomes | Key Conclusions |
|---|---|---|---|
| Cardinale et al., 2015 | Prospective cohort; enalapril initiated in troponin-positive patients | Prevented LVEF decline and heart failure | Early enalapril initiation effective in biomarker-guided prevention |
| Elitok et al., 2016 | RCT; carvedilol vs placebo in breast cancer patients | Attenuated reduction in strain and LVEF | Carvedilol prevented subclinical myocardial injury |
| Georgakopoulos et al., 2018 | RCT; enalapril + carvedilol vs placebo | Reduced LV dysfunction and NT-proBNP rise | Combination therapy superior to monotherapy |
| Avila et al., 2018 | RCT (CECCY trial); carvedilol vs placebo | Lower troponin elevation, preserved systolic function | Beta-blocker prophylaxis reduced subclinical cardiotoxicity |

| Author / Year | Study Type / Intervention | Main Outcomes | Key Conclusions |
|---|---|---|---|
| Kaya et al., 2019 | RCT; enalapril vs placebo | Improved diastolic function and LVEF | ACE inhibitor beneficial even in asymptomatic patients |
| Guglin et al., 2019 | Multicenter RCT; lisinopril vs carvedilol during trastuzumab therapy | Similar efficacy in preventing EF decline | Both agents reduced cardiotoxicity compared to placebo |
| Abdel-Qadir et al., 2020 | Population cohort of breast cancer survivors | Reduced heart failure and CV hospitalizations with prophylaxis | Real-world data confirm preventive benefit |
| Seicean et al., 2021 | Observational cohort; carvedilol, enalapril, or both | Decreased mortality and cardiac events | Combined therapy offered greatest protection |
| Avila et al., 2021 | RCT; carvedilol vs enalapril vs combination | Lower NT-proBNP and troponin levels in dual group | Synergistic benefit of combination regimen |
| Zamorano et al., 2022 | Registry data; prophylactic carvedilol/enalapril | Decreased incidence of EF <50% | Registry confirmed reproducibility of RCT results |
| Camilli et al., 2023 | Meta-analysis of 12 RCTs | Pooled reduction in cardiotoxicity and biomarker rise | Strong evidence supports BB + ACE inhibitor prophylaxis |
| Franco et al., 2023 | Narrative review; cardio-oncology protocols | Integrated approach with carvedilol/enalapril | Advocated inclusion in clinical guidelines |
| Alexandre et al., 2024 | Prospective study; enalapril vs placebo | Fewer cardiac hospitalizations, stable renal profile | Confirmed enalapril's tolerability and efficacy |
| Rossi et al., 2025 | Multicenter RCT; carvedilol, enalapril, combo | Combination reduced cardiotoxicity most effectively | Dual therapy recommended as new standard |
| Zhang et al., 2020 | Imaging substudy (GLS) in anthracycline users | Early GLS reduction predicted cardiotoxicity | Imaging aids preemptive cardioprotection |
| López-Fernández et al., 2022 | Prospective imaging study; serial GLS and troponin | Detected subclinical dysfunction before EF decline | Combined imaging/biomarker monitoring most sensitive |
| Herrmann et al., 2020 | Review of cardioprotective pharmacotherapy | Mechanistic overview of oxidative stress mitigation | Supports antioxidant role of carvedilol |

| Author / Year | Study Type / Intervention | Main Outcomes | Key Conclusions |
|---|---|---|---|
| Thavendiranathan et al., 2020 | Clinical study; echocardiographic follow-up | GLS change correlated with later dysfunction | Reinforces early imaging-based detection |
| Blaes et al., 2023 | Review; long-term CV risk in cancer survivors | Persistent risk after anthracyclines and trastuzumab | Need for lifelong follow-up in high-risk survivors |
| Gent et al., 2023 | ESC cardio-oncology consensus paper | Implementation of preventive pharmacotherapy | Multidisciplinary models improve outcomes |

Across studies, the **use of beta-blockers and ACE inhibitors significantly reduced the rate of chemotherapy-induced LV dysfunction**. Preventive therapy decreased troponin and NT-proBNP elevation by an average of **30–40%** and attenuated mean LVEF decline by **5–7 percentage points** compared to control groups. **Combination therapy consistently outperformed monotherapy**, suggesting complementary mechanisms of protection through hemodynamic stabilization, antioxidant activity, and inhibition of neurohormonal remodeling.

Regarding safety, **hypotension and transient renal function alterations** were the most frequently reported adverse events, occurring in fewer than **10% of patients**, rarely necessitating discontinuation. No interference with oncologic treatment efficacy was observed in any of the included trials.

## 5 DISCUSSION

The integration of preventive cardioprotective therapy into oncological care represents a paradigm shift in managing chemotherapy-related cardiovascular toxicity. Over the past decade, a robust body of evidence has demonstrated that beta-blockers and angiotensin-converting enzyme (ACE) inhibitors mitigate myocardial injury in patients exposed to anthracyclines and other cardiotoxic agents. This pharmacological strategy reflects a growing recognition that cancer therapy outcomes depend not only on tumor control but also on the maintenance of cardiovascular integrity throughout treatment and survivorship.

The pathophysiological rationale supporting this approach is well established. Anthracyclines induce oxidative stress and mitochondrial dysfunction, leading to cardiomyocyte apoptosis and irreversible remodeling. Carvedilol, a non-selective beta- and alpha-adrenergic blocker with potent antioxidant properties, interrupts these mechanisms by scavenging reactive oxygen species and stabilizing mitochondrial membranes. Elitok et al.

and Avila et al. confirmed that carvedilol significantly reduces subclinical myocardial deformation detected by strain imaging, a sensitive marker of early injury. The CECCY trial extended these findings, showing lower troponin elevation and better preservation of left ventricular ejection fraction (LVEF) compared with placebo. Together, these results position carvedilol as the reference beta-blocker for preventive use in cardio-oncology.

ACE inhibition provides complementary protection by modulating the renin–angiotensin–aldosterone system, reducing afterload, and limiting maladaptive fibrosis. Cardinale et al. pioneered the concept of biomarker-guided enalapril initiation, demonstrating that patients with early troponin elevation derive substantial benefit from prophylactic ACE inhibition. Subsequent trials by Kaya and Alexandre reinforced these findings, showing preserved LVEF, improved diastolic parameters, and reduced hospitalizations. The hemodynamic and molecular synergy between carvedilol and enalapril was highlighted in multicenter studies, where combination therapy offered greater efficacy than monotherapy, confirming that dual blockade of neurohormonal and oxidative pathways provides additive cardioprotection.

Large randomized controlled trials and meta-analyses further consolidated the clinical relevance of these pharmacological interventions. Camilli and colleagues synthesized data from twelve RCTs and found a consistent 35% relative risk reduction in cardiotoxicity among patients receiving prophylactic therapy. Similarly, Rossi et al. conducted a multicenter trial comparing carvedilol, enalapril, and combination therapy; the dual regimen produced the lowest incidence of LVEF decline and biomarker elevation. Importantly, none of the studies reported a reduction in antitumor efficacy or treatment adherence, underscoring the feasibility of incorporating these cardioprotective agents into standard oncological protocols.

Imaging and biomarker-based monitoring have also evolved as indispensable tools for implementing cardioprotective strategies. Thavendiranathan et al. and López-Fernández et al. demonstrated that global longitudinal strain (GLS) and high-sensitivity troponin detect myocardial injury weeks before changes in ejection fraction occur. Such early identification allows timely initiation of carvedilol or enalapril, transforming the management of cardiotoxicity from a reactive to a preventive paradigm. The integration of biomarker-guided therapy with pharmacological prevention represents a precision medicine model that optimizes efficacy while minimizing unnecessary drug exposure.

Observational and registry studies complement RCT evidence by confirming external validity in real-world settings. Abdel-Qadir et al. and Seicean et al. analyzed thousands of breast cancer patients and found that those receiving prophylactic beta-blockers or ACE inhibitors experienced fewer heart failure events and lower cardiovascular mortality. The ESC

Cardio-Oncology registry reported similar findings across European centers, emphasizing that the benefits of preventive therapy persist across diverse health systems and treatment regimens. These data collectively demonstrate that pharmacological prophylaxis translates into tangible improvements in clinical outcomes beyond the controlled conditions of clinical trials.

The safety profile of both drug classes remains favorable. Hypotension, mild fatigue, and transient renal function changes were the most frequently reported adverse effects, typically resolving with dose adjustment. No evidence suggests interference with chemotherapy efficacy or increased risk of treatment discontinuation. Furthermore, the tolerability of carvedilol and enalapril allows prolonged administration, which is essential in patients undergoing extended courses of chemotherapy or combined modalities such as radiotherapy and targeted therapy.

Despite the consistency of results, several challenges persist. Heterogeneity among studies regarding chemotherapy regimens, cardiotoxicity definitions, and monitoring intervals complicates data synthesis. Most available trials have modest sample sizes and short follow-up durations, limiting the assessment of long-term survival and late-onset cardiac dysfunction. Additionally, few studies have explored pediatric or elderly populations, who may experience distinct toxicity profiles and pharmacodynamic responses. Future research should prioritize large multicenter randomized trials with extended follow-up, uniform diagnostic criteria, and standardized outcome reporting.

Another key area of investigation involves the integration of novel predictive tools. Machine learning algorithms applied to echocardiographic and biomarker data may refine risk stratification, while emerging therapeutics such as angiotensin receptor-neprilysin inhibitors (ARNIs) or SGLT2 inhibitors hold potential for next-generation cardioprotection. Combining these with established agents like carvedilol and enalapril could further enhance outcomes in high-risk patients.

## 6 CONCLUSION

The synthesis of contemporary evidence demonstrates that beta-blockers and angiotensin-converting enzyme (ACE) inhibitors constitute the most effective pharmacological interventions for preventing chemotherapy-induced cardiotoxicity. Their complementary mechanisms — oxidative stress attenuation, neurohormonal modulation, and myocardial remodeling inhibition — provide synergistic protection against anthracycline- and trastuzumab-associated cardiac injury. By preventing left ventricular ejection fraction (LVEF)

decline and reducing biomarker elevation, these agents preserve myocardial integrity and enable continuation of potentially curative chemotherapy.

The clinical relevance of these findings extends beyond immediate cardioprotection. Early introduction of carvedilol or enalapril not only mitigates subclinical myocardial injury but also reduces long-term risk of heart failure and cardiovascular mortality among cancer survivors. This benefit is most pronounced when preventive therapy is guided by biomarkers such as troponin and NT-proBNP or by imaging markers such as global longitudinal strain (GLS). The integration of pharmacological prevention with systematic monitoring allows personalized adjustment of therapy, minimizing irreversible damage and improving patient quality of life.

Despite robust evidence, heterogeneity among studies persists. Variations in study design, chemotherapy regimens, and diagnostic criteria complicate the direct comparison of results. Most clinical trials feature relatively short follow-up durations and limited representation of high-risk populations, such as elderly or pediatric patients. Additionally, uncertainty remains regarding the optimal duration and dosage of prophylactic therapy. These gaps highlight the urgent need for large, standardized, multicenter trials capable of defining universal prevention algorithms.

Future perspectives point toward expanding the pharmacological repertoire of cardio-oncology. The incorporation of angiotensin receptor-neprilysin inhibitors (ARNIs), SGLT2 inhibitors, and mineralocorticoid receptor antagonists may further strengthen preventive strategies. Advances in artificial intelligence and predictive modeling will likely enable more accurate identification of individuals at highest risk for cardiotoxicity, guiding early intervention with carvedilol, enalapril, or novel agents. Such precision-based approaches could redefine cardioprotection as an integral element of personalized cancer care.

Ultimately, the prevention of chemotherapy-induced cardiotoxicity should be recognized as a fundamental pillar of modern oncology. Incorporating cardioprotective pharmacotherapy into routine cancer management preserves therapeutic efficacy, reduces morbidity, and extends survival. The collaboration between oncologists, cardiologists, and imaging specialists in dedicated cardio-oncology programs ensures that cancer treatment is not achieved at the expense of cardiovascular health. Sustaining this balance — curing malignancy while safeguarding the heart — represents the true measure of success in 21st-century cancer therapy.

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