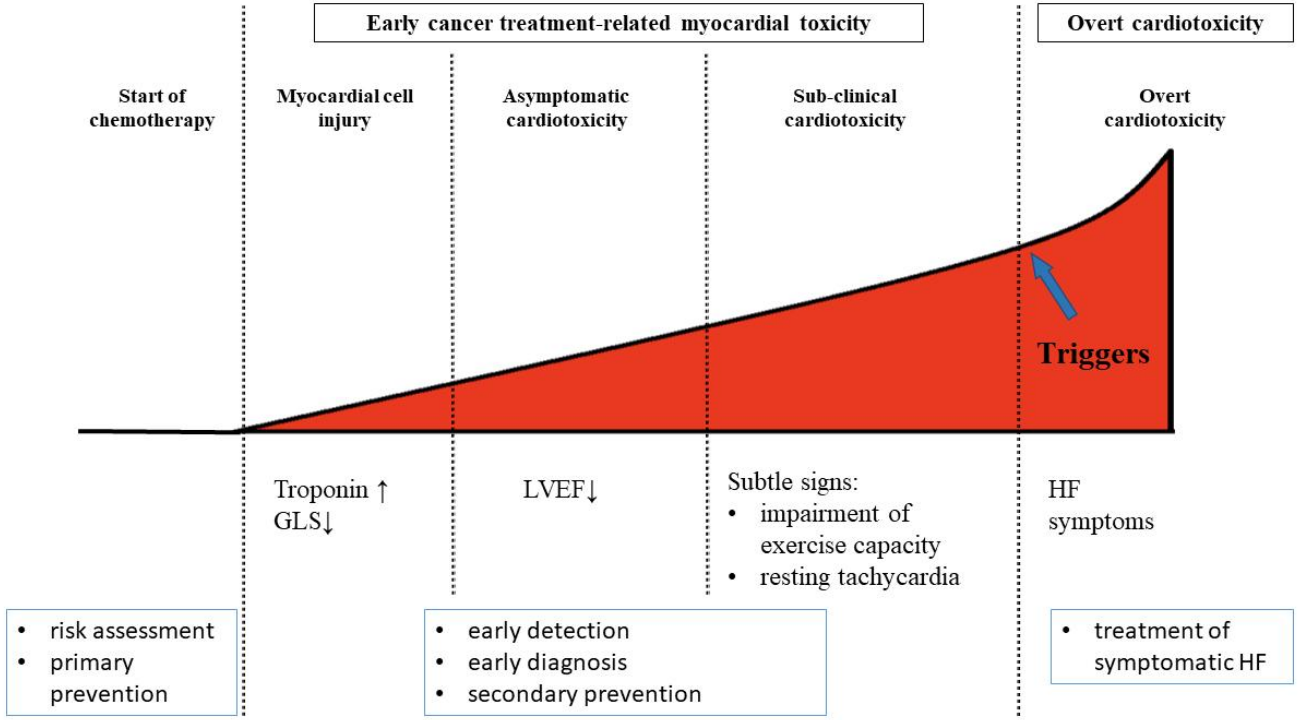
Supplementary Figure 1: Schematic diagram of disease progression, symptoms and possible management strategies for anticancer therapy-induced cardiotoxicity. GLS: global longitudinal strain; LVEF: left ventricular ejection fraction; HF: heart failure.



Supplementary Table 1: Prospective clinical trials of prevention in patients with cancer

Clinical trials	Included population	Treatment for the population	Types of prevention	Interventions	Primary endpoint	Monitoring tools	Main results
PRADA, 2016[8]	130 early breast cancer patients	Anthracycline (22% of cases were combined with trastuzumab)	Primary prevention	1:1:1:1, metoprolol, candesartan, and metoprolol combination with candesartan or placebo	Change in LVEF from baseline to completion of adjuvant anticancer therapy	CMR	Candesartan positive, LVEF absolute value change: 2.6% in the placebo group and 0.8% in the candesartan group (p=0.026)
MANTICORE-101, 2017[10]	94 HER2-positive early breast cancer patients	Trastuzumab (12-33% of them were combined with Anthracycline)	Primary prevention	1:1:1, perindopril, bisoprolol, or placebo	LVEF change from baseline to completion of 17 cycles of trastuzumab	CMR	Positive, bisoprolol and perindopril compared with placebo, which showed a small decrease in LVEF (–1% vs. –3% vs. –5%, p=0.001)
Guglin et al., 2019[11]	468 HER2-positive early breast cancer patients	Trastuzumab (40% of them were combined with anthracycline)	Primary prevention	1:1:1, carvedilol, lisinopril or placebo	LVEF decrease >10%, or >5% if below 50%	UCG (59.7%) or MUGA (40.3%)	The overall population was negative. For patients receiving anthracyclines, the event rates were higher in the placebo group (47%) than in the lisinopril (37%) and the carvedilol (31%) groups. Cardiotoxicity-free survival was longer with both carvedilol (HR, 0.49, p=0.009) and lisinopril (HR, 0.53, p=0.015)
CECCY, 2018[14]	200 HER2-negative breast cancer patients	Anthracycline	Primary prevention	1:1, carvedilol or placebo	≥10% reduction in LVEF at 6 months	UCG	Negative, decreased LVEF: placebo group 13.5%, carvedilol group 14.5% (p=1.00)
Boekhout et al., 2016[15]	206 patients with HER2-positive early breast cancer	Anthracycline-containing chemotherapy followed by trastuzumab	Primary prevention	1:1, candesartan or placebo	Decrease in LVEF greater than 15% compared with baseline or a decrease to an absolute value of LVEF below 45%	UCG or MUGA	Negative, decreased LVEF: 19% in the candesartan group versus 16% in the placebo group (p=0.58)

Janbabai et al., 2017[9]	69 newly diagnosed patients with metastatic tumor	Anthracycline	Primary prevention	1:1, enalapril or none	LVEF change (baseline compared with 6 months after randomization)	UCG	Positive, LVEF change: no decrease in the enalapril group (p=0.58) and a significant decrease in the placebo group (p=0.001)
OVERCOME, 2013[16]	90 patients with acute leukemia or malignant hemopathies	Undergoing autologous hematopoietic stem cell transplantation (HSCT)	Primary prevention	1:1, enalapril+carvedilol or placebo	Absolute change in LVEF (baseline compared with 6 months)	UCG (34.4%) or CMR (65.6%)	Positive, LVEF absolute value change: no change in the intervention group but - 3.1% (echocardiography, p=0.035) and - 3.4% (CMR, p=0.09) in the control group
Acar et al., 2011[17]	40 cancer patients	Anthracycline	Primary prevention	1:1, statins or none	LVEF＜50% at 6 months	UCG	Positive, LVEF change: no decrease in the statin group (p=0.144) and a significant decrease in the control group (p<0.0001))
Akpek et al., 2015[12]	83 female breast cancer patients	Anthracycline-containing chemotherapy	Primary prevention	1:1, spironolactone or placebo	NM	ECG, UCG and cardiac biomarkers	Positive, diastolic functional grade: no change in the spironolactone group (p=0.096) but deterioration in the control group (p<0.001)
Cardinale et al., 2006[18]	114 cancer patients with elevated troponin I	High-dose chemotherapy	Secondary prevention	1:1, enalapril or none	The absolute value of LVEF decreased by 10% to below 50%	UCG	Positive, the incidence of the primary endpoint: enalapril (0%), control (43%), p<0.001
Cardinale et al., 2010[19]	201 cancer patients with an LVEF ≤45% due to AC	Anthracycline-containing chemotherapy	Secondary prevention	Enalapril ± carvedilol (only enalapril, n=72; combination, n=129)	LVEF response to HF therapy	UCG	Responders (n=85, 42%); partial responders (n=26,13%), and nonresponders (n=90, 45%)

ACEI, Angiotensin-converting enzyme inhibitor; ARB, Angiotensin II receptor blocker; LVEF, Left ventricular ejection fraction; CMR, Cardiac magnetic resonance; MUGA, Multiple gate acquisition radionuclide imaging; AC, Anthracycline-induced cardiomyopathy; NM, Not mentioned; HF, Heart failure