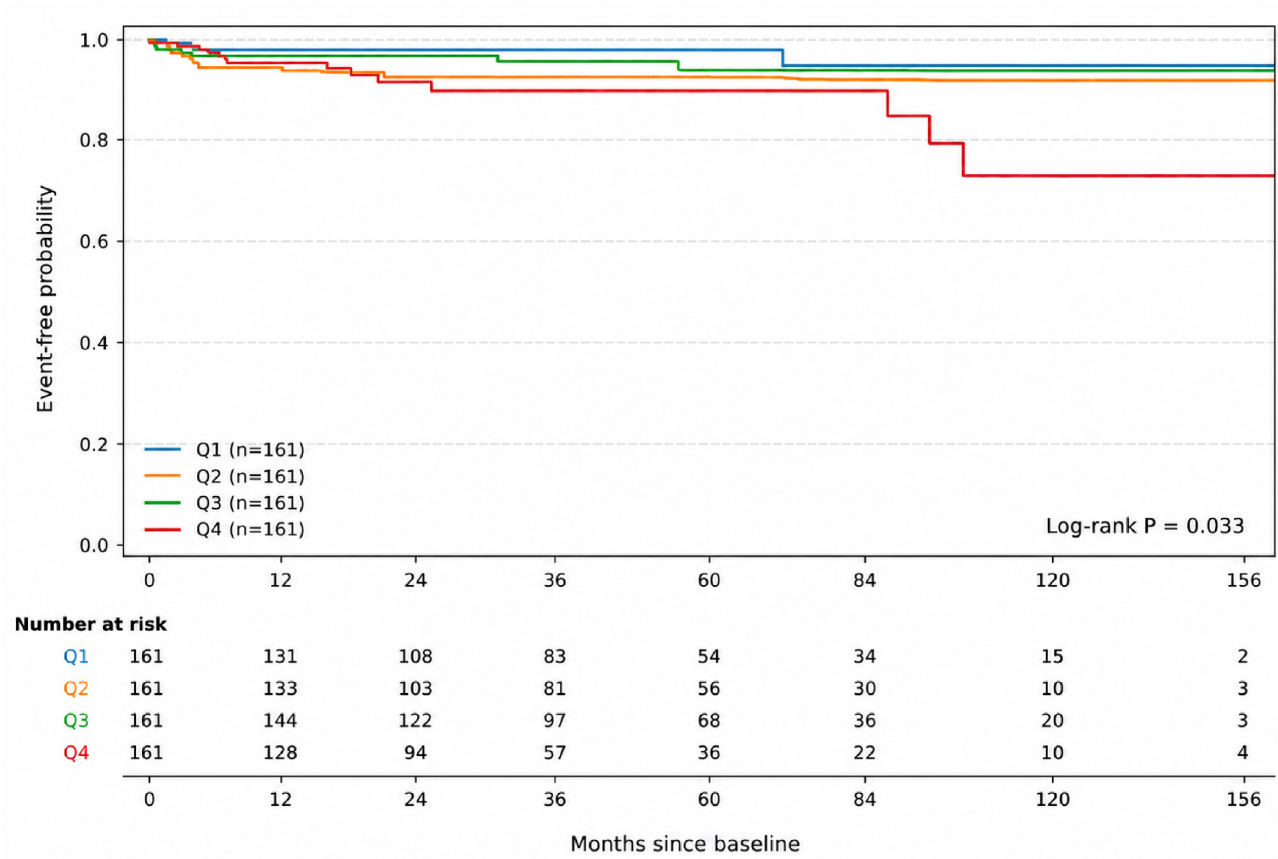
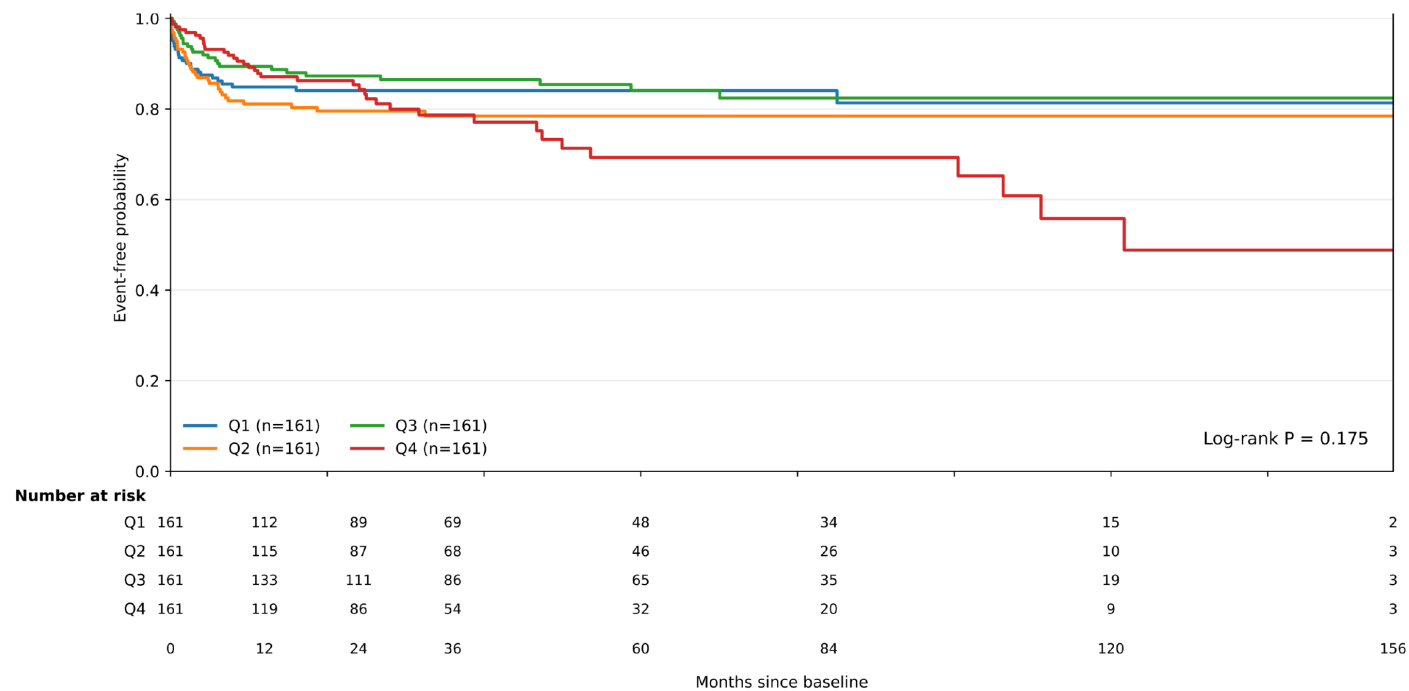




Supplementary Figure S1A. Echocardiographic abnormality-free survival according to cumulative doxorubicin-equivalent dose quartiles. Kaplan-Meier curves show time to incident echocardiographic abnormality in Q1-Q4. Numbers at risk are shown below the plot. Differences among quartiles were assessed using the log-rank test (P=0.033).



Supplementary Figure S1B. Echocardiographic-or-cardiac-enzyme abnormality-free survival according to cumulative doxorubicin-equivalent dose quartiles. Kaplan-Meier curves show time to the sensitivity endpoint comprising incident echocardiographic or cardiac enzyme abnormality and excluding ECG abnormalities. Numbers at risk are shown below the plot. The log-rank test showed no statistically significant difference among quartiles ($P=0.175$).

Age (P interaction = 0.459)

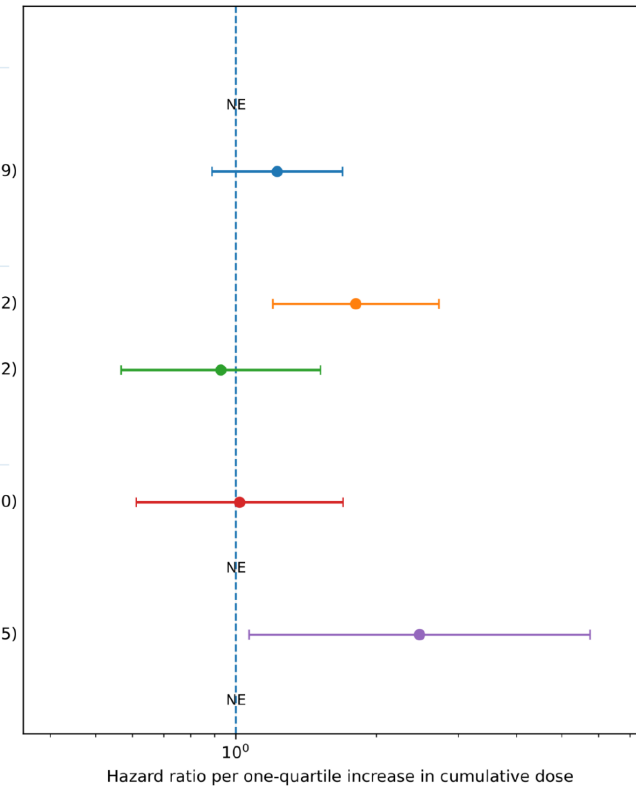
<5 years	242 / 3	NE
≥5 years	402 / 34	1.23 (0.89-1.69)

Sex (P interaction = 0.044)

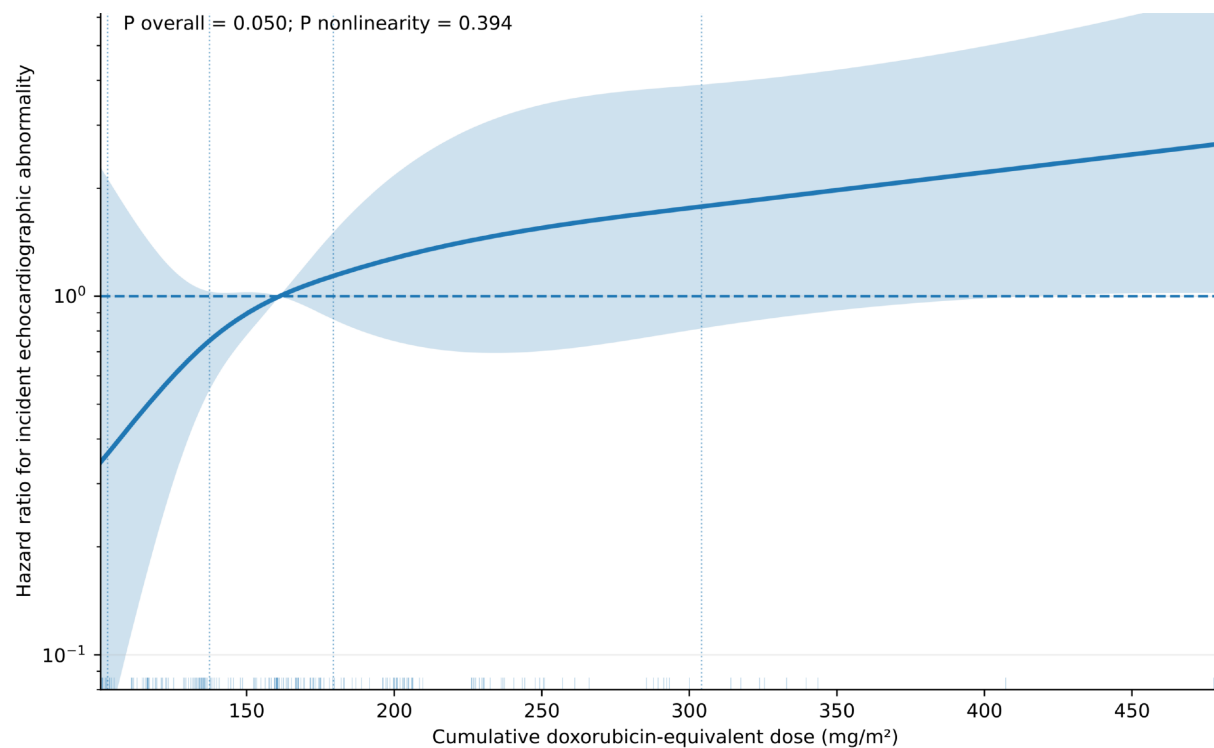
Male	411 / 25	1.81 (1.20-2.72)
Female	233 / 12	0.93 (0.57-1.52)

Diagnosis (P interaction = 0.101)

Hematologic malignancy	164 / 18	1.02 (0.61-1.70)
Neuroblastoma	121 / 3	NE
Sarcoma	230 / 12	2.48 (1.07-5.75)
Other solid tumor	129 / 4	NE



Supplementary Figure S2. Subgroup analysis of incident echocardiographic abnormality. Forest plot showing hazard ratios (HRs) for incident echocardiographic abnormality associated with each one-quartile increase in cumulative doxorubicin-equivalent dose across prespecified subgroups. Subgroups were defined by age group, sex, and primary diagnosis. Hazard ratios were estimated using Cox proportional hazards models. P values for interaction assessed potential effect modification. NE indicates not estimable because fewer than five events were available in the corresponding subgroup. Interaction P values were nominal and the subgroup analyses were exploratory.



Supplementary Figure S3. Restricted cubic spline analysis of the association between cumulative doxorubicin-equivalent dose and incident echocardiographic abnormality. Restricted cubic spline modelling was performed using Cox proportional hazards regression with four knots and adjustment for age at diagnosis and sex. The reference dose was 161.1 mg/m², corresponding to the median cumulative doxorubicin-equivalent dose. The solid line represents the estimated hazard ratio and the shaded area the 95% confidence interval; the dashed horizontal line indicates HR=1.0. **The overall association was borderline (P=0.050), and there was no statistically significant evidence of nonlinearity (P for nonlinearity=0.394). Confidence intervals widened at higher doses, limiting inference regarding the precise shape of the exposure-response relationship.**