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Risk factors for incident cardiovascular and cerebrovascular disease among cancer survivors: a discrete-time cohort study

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Abstract

Background

Cancer survivors may develop cardiovascular and cerebrovascular disease through shared cardiometabolic risk, functional vulnerability, and treatment-related exposures. We evaluated four clinically prespecified risk domains in adults with cancer who were free of cardiovascular and cerebrovascular disease at baseline.

Methods

This longitudinal cohort analysis included 183 adults with cancer followed at discrete 3-year and 5-year assessments. The analytic data were expanded to person-period records and analyzed using complementary log-log discrete-time survival models with cluster-robust standard errors. Age, sex, smoking, drinking, and continuous BMI were retained in the demographic core. Asian BMI categories were examined as a prespecified sensitivity analysis without replacing the continuous BMI analysis.

Results

Forty-three incident events occurred (27 at 3 years and 16 at 5 years); the observed cumulative event proportions were 14.8% and 23.5%, respectively. In the demographic core model, the discrete-time hazard ratio (DTHR) was 1.45 per 10-year increase in age (95% CI, 0.99–2.14; P=.058) and 2.19 per 5-kg/m² increase in BMI (95% CI, 1.31–3.66; P=.003). Mobility severity was associated with higher risk (DTHR, 1.24 per point; 95% CI, 1.01–1.51; P=.037). Each additional baseline comorbidity was associated with higher risk in the parsimonious model (DTHR, 1.55; 95% CI, 1.03–2.35; P=.037). In the Asian BMI sensitivity analysis, obesity versus normal BMI was associated with higher risk (DTHR, 3.73; 95% CI, 1.54-9.00; P=.003).

Conclusions

Among the most consistent risk indicators were elevated BMI, mobility limitations, and cumulative cardiometabolic comorbidities. However, the study's two-visit design, lack of precise timing for mortality events, and limited number of observed outcomes necessitate cautious interpretation and validation through external studies.

Background

Cardiovascular and cerebrovascular disease (CVD) is a major cause of morbidity among individuals living with and beyond cancer (1). Cancer survivors may present with typical vascular risk factors, in addition to experiencing inflammation, thrombosis, metabolic disturbances, and treatment-related

cardiovascular injury. This cumulative burden has direct implications for survivorship care, as effective prevention relies on early risk recognition, control of modifiable cardiometabolic factors, maintenance of physical function, and monitoring of treatment-related toxicity. Consequently, contemporary cardio-oncology guidelines recommend a risk assessment approach that integrates baseline cardiovascular health with cancer treatment exposure and survivorship follow-up (2). Supporting this rationale, the ARIC cohort study found a higher risk of composite CVD among cancer survivors compared to adults without cancer, even after adjusting for traditional risk factors (3). However, the evidence regarding the determinants of CVD after cancer remains heterogeneous. For instance, a meta-analysis of population-based cohorts revealed an overall higher stroke risk among cancer survivors, while a Japanese prospective study observed no sustained excess stroke risk for all cancers, identifying the clearest elevation during the first 1–3 months post-cancer diagnosis (4, 5). Recent registry data further indicate that cardiovascular outcomes vary by cancer type and treatment agent, showing increased heart failure and specific treatment-related risks, but not a uniform increase across all vascular outcomes (6). These findings underscore that prevention cannot rely on a single cancer-survivor risk estimate; instead, it necessitates the identification of patient-level factors that are relevant across diverse survivorship settings.

Several potentially actionable domains merit integrated evaluation. In Asian populations, body mass index (BMI) may inadequately capture adiposity-related cardiometabolic risk when assessed using conventional Western thresholds. Consequently, Asian-specific guidelines advocate for the use of lower BMI thresholds, alongside consideration of metabolic abnormalities and, where feasible, measures of central adiposity (7). Prospective studies conducted in Chinese cohorts have revealed graded associations between body size, metabolic dysfunction, and cardiovascular disease (CVD) risk (8, 9).

Several potentially actionable domains merit integrated evaluation. In Asian populations, body mass index (BMI) may inadequately capture adiposity-related cardiometabolic risk when assessed using conventional Western thresholds. Consequently, Asian-specific guidelines advocate for the use of lower BMI thresholds, alongside consideration of metabolic abnormalities and, where feasible, measures of central adiposity (7). Prospective studies conducted in Chinese cohorts have revealed graded associations between body size, metabolic dysfunction, and CVD risk (8, 9). Functional vulnerability may add information that is not captured by BMI or comorbidity counts. Activities of daily living (ADLs)/Instrumental of daily living (IADLs) limitation and other functional dependence have been associated with subsequent CVD in Chinese cohorts (10), and higher objectively measured physical activity has been associated with lower CVD risk among cancer survivors (11). These findings support a prevention framework that combines blood pressure, glucose, lipid, and weight management with assessment of mobility and function, but the independent contribution of these domains among cancer patients who are free of CVD at baseline has not been fully characterized.

We therefore investigated four prespecified domains associated with incident CVD among adults with cancer who without CVD at baseline: demographic and lifestyle factors, cardiometabolic comorbidities, functional status, and cancer treatment indicators. Because follow-up was recorded only at 3-year and 5-

year visits, the primary analysis used discrete-time survival methods rather than treating the recorded visit time as an exact event time. Our aim was to identify clinically interpretable risk factors that can inform integrated cardio-oncology, primary-care, neurology, and rehabilitation prevention strategies.

Methods

Study design and analytic population

The China Health and Retirement Longitudinal Study (CHARLS) initiated in 2011 and serves as a nationwide survey focusing on individuals in China who are 45 years old or older. High-quality data is obtained by conducting structured interviews using a uniform questionnaire. A probability-proportionate-to-size multistage stratified sampling approach is utilized to select participants. Wave 1 of the nationwide survey in 2011 included 150 counties and districts from 28 provinces, providing comprehensive geographical and socioeconomic representation. Follow-up surveys have been carried out every two years: Wave 2 (2013–2014), Wave 3 (2015–2016), Wave 4 (2017–2018), and Wave 5 (2019–2020). The dataset incorporates individual weighting variables to ensure it remains nationally representative. Further details about the CHARLS study design can be found in earlier publications (12). Informed consent was obtained from all participants, and the study protocol received approval from Peking University's Ethical Review Committee (approval number: IRB00001052–11,015). All methods complied with institutional and national ethical regulations, the Declaration of Helsinki (1964, with amendments), and similar guidelines. The study also followed the STROBE reporting standard (13).

The research focused on individuals aged 45 and older who were diagnosed with cancer and did not have a CVD diagnosis during Wave3. In the beginning of Wave 3, 25,586 participants were included. Exclusions were made for individuals without cancer diagnosis at wave3 (n = 25254), those with a CVD diagnosis (n = 96), those with younger than 45 years (n = 2), and those without follow-up visits (n = 51). Consequently, our analysis included 183 participants who satisfied the eligibility requirements (Fig. 1).

Assessment of outcomes

The main focus of this study was the occurrence of CVD. In waves 4 and 5 of the CHARLS study, participants were questioned about whether a doctor had ever diagnosed them with a heart condition or stroke. They were additionally inquired about their present use of therapies for heart issues or stroke, including options like traditional Chinese medicine, Western medicine, chemotherapy, or opting for no treatment. Participants were considered to have CVD if they mentioned a physician's diagnosis of a cardiovascular issue or stroke, or if they indicated receiving treatments related to these conditions.

Risk Factors

All accessible factors in CHARLS were analyzed using data from Wave 3. The following data was collected in this study: (1) demographics: age, gender, BMI, smoking and alcohol consumption status; (2) chronic diseases: hypertension, diabetes, dyslipidemia; (3) physical function: activities of daily living (ADLs), instrumental activities of daily living (IADLs), other function limitations, 7 item mobility, upper body mobility and lower body mobility; (4) treatment for cancer: medication, chemotherapy or surgery.

Statistical Analysis

Baseline characteristics were summarized separately according to the occurrence of incident CVD. Frequencies and percentages were used to present categorical variables, while continuous variables were described using means with standard deviations or medians with interquartile ranges, depending on the context. The primary demographic model included age, sex, smoking status, alcohol consumption, and continuous BMI. Age was modeled per 10-year increase and BMI per 5-kg/m² increase. Domain-specific models additionally included comorbidities (hypertension, diabetes mellitus, and dyslipidemia), functional measures (ADL, IADL and other functional limitations), and treatment variables (surgery, radiotherapy, and the cancer-medication indicator), respectively. Each domain-specific model was adjusted for the demographic core variables.

Considering CVD status was assessed only at the scheduled 3- and 5-year visits and exact event dates were unavailable, a discrete-time survival analysis was performed using a person-period data structure. Discrete-time survival models are appropriate when event occurrence is known only within prespecified follow-up intervals and can accommodate interval-specific baseline hazards without requiring exact event times (14, 15). Follow-up was divided into two intervals: baseline to 3 years and 3 to 5 years. Participants with an event at 3 years contributed one record, whereas those who remained event-free at 3 years and were followed to 5 years contributed two records. Follow-up ended at the first documented CVD event or the last available assessment. Associations between baseline factors and incident CVD were estimated using complementary log-log discrete-time survival regression. A follow-up interval indicator was included to allow the baseline hazard to vary between intervals. Cluster-robust standard errors were calculated at the participant level to account for repeated observations (16). Results are reported as discrete-time hazard ratios (DTHRs) with 95% confidence intervals (CIs). Because 43 events occurred among 183 participants, a fully adjusted model including all candidate variables was not used as the primary model. Instead, variables were prespecified according to clinical relevance and the four exposure domains. A parsimonious model was additionally fitted using the numbers of cardiometabolic comorbidities, functional deficits, and treatment indicators.

All statistical tests were conducted using R software version 4.3.1 (http://www.R-project.org/), with a P-value below 0.05 indicating statistical significance. Given the limited number of events, interpretation focused primarily on effect estimates and 95% CIs rather than P values alone.

Sensitivity analyses

Prespecified sensitivity analyses were performed to examine the robustness of the findings to alternative representations of functional status and BMI. Mobility severity was evaluated as an alternative measure of functional status. Continuous BMI was replaced by Asian-specific BMI categories, with normal weight used as the reference category. The categories were defined as underweight (< 18.5 kg/m²), normal weight (18.5–22.9 kg/m²), overweight (23.0–27.4 kg/m²), and obesity (≥ 27.5 kg/m²), based on contemporary Asian and international guidance (7). Both analyses employed the same complementary log-log discrete-time survival model, incorporating participant-level cluster-robust standard errors.

Results

Participant Flow and Incident CVD Events

The analytic cohort consisted of 183 adults with cancer who were free of CVD at baseline. Over the follow-up period, 43 incident CVD events were recorded: 27 by the 3-year assessment and an additional 16 by the 5-year assessment. The cumulative event proportions observed were 14.8% at 3 years and 23.5% at 5 years. At the final recorded assessment, 140 participants remained free of CVD. These estimates reflect the observed event occurrence within the two scheduled follow-up periods and should not be interpreted as exact-time incidence rates.

Baseline Characteristics

Baseline characteristics are summarized in Table 1. Participants who subsequently developed CVD had a higher median BMI compared to those who remained event-free (25.1 vs. 23.1 kg/m²). Additionally, hypertension and diabetes were more prevalent among participants who experienced CVD events compared to those who did not (39.5% vs. 22.9% and 30.2% vs. 11.4%, respectively). These differences are descriptive in nature and do not account for the interval-based follow-up structure or covariate adjustment; thus, they should not be interpreted as evidence of independent associations.

Table 1
Baseline characteristics of the analytic cohort.

Characteristic	Overall (N = 183)	No CVD (n = 140)	CVD (n = 43)	P
Age, years	58.0 (51.0–64.0)	58.0 (51.0–63.0)	58.0 (52.0–69.0)	0.113
BMI, kg/m²	23.9 (20.4–26.6)	23.1 (20.0-26.1)	25.1 (21.5–28.1)	0.025
Sex (Man)	51 (27.9%)	35 (25.0%)	16 (37.2%)	0.118
Smoking				0.501
Never	135 (73.8%)	106 (75.7%)	29 (67.4%)	
Former	19 (10.4%)	14 (10.0%)	5 (11.6%)	
Current	29 (15.8%)	20 (14.3%)	9 (20.9%)	
Drinking				0.189
Never	123 (67.2%)	99 (70.7%)	24 (55.8%)	
Former	34 (18.6%)	23 (16.4%)	11 (25.6%)	
Current	26 (14.2%)	18 (12.9%)	8 (18.6%)	
Hypertension	49 (26.8%)	32 (22.9%)	17 (39.5%)	0.031
Diabetes	29 (15.8%)	16 (11.4%)	13 (30.2%)	0.003
Dyslipidemia	32 (17.5%)	21 (15.0%)	11 (25.6%)	0.110
ADLs deficit	45 (24.6%)	32 (22.9%)	13 (30.2%)	0.326
IADLs deficit	60 (32.8%)	47 (33.6%)	13 (30.2%)	0.683
Other function deficit	137 (74.9%)	102 (72.9%)	35 (81.4%)	0.259
Cancer medication	110 (60.1%)	83 (59.3%)	27 (62.8%)	0.681
Surgery	75 (41.0%)	59 (42.1%)	16 (37.2%)	0.565
Radiotherapy	46 (25.1%)	37 (26.4%)	9 (20.9%)	0.467

Demographic Core Model

In the demographic core model, age demonstrated a positive association with the estimated discrete-time hazard of incident CVD, although the CIs encompassed the null value DTHR, 1.45 per 10-year increase; 95% CI, 0.99–2.14; P = 0.058). In contrast, continuous BMI exhibited a more robust and precise positive association, with each 5-kg/m² increase in BMI corresponding to a 2.19-fold higher discrete-time hazard (95% CI, 1.31–3.66; P = 0.003). The estimates for sex, smoking status, and drinking status were imprecise and did not provide clear evidence of independent associations in this cohort.

Cardiometabolic Comorbidity and Functional-Status Models

After adjustment for the demographic core, the point estimates for individual cardiometabolic comorbidities were greater, but the CIs were wide and crossed the null value. The DTHR was 1.21 for hypertension (95% CI, 0.58–2.51; P = 0.610), 1.76 for diabetes (95% CI, 0.83–3.75; P = 0.144), and 1.69 for dyslipidemia (95% CI, 0.83–3.43; P = 0.148). These estimates are compatible with increased risk but are not sufficiently precise to establish independent associations. Similarly, none of the individual functional indicators showed clear evidence of an association: ADLs deficit, DTHR 1.48 (95% CI, 0.65–3.38; P = 0.346); IADLs deficit, DTHR 0.78 (95% CI, 0.40–1.53; P = 0.472); and other functional limitation, DTHR 1.54 (95% CI, 0.61–3.91; P = 0.364).

Cancer-Treatment Models

None of the treatment indicators showed clear evidence of an association with incident CVD: cancer-medication indicator, DTHR 1.26 (95% CI, 0.58–2.74; P = 0.554); surgery, DTHR 0.73 (95% CI, 0.34–1.54; P = 0.410); and radiotherapy, DTHR 0.81 (95% CI, 0.33–1.95; P = 0.635). The imprecision of these estimates limits conclusions regarding treatment-related risk.

Sensitivity Analysis

Within the prespecified mobility model, higher mobility-severity scores were linked to an increased estimated discrete-time hazard. Each one-point increase in mobility severity corresponded to a 24% higher estimated hazard (DTHR, 1.24; 95% CI, 1.01–1.51; P = 0.037). This association was statistically compatible with a positive relationship, although the confidence interval was relatively close to the null.

Furthermore, the categorical BMI analysis was directionally consistent with the findings of the primary continuous BMI analysis (refer to Table 2 and Fig. 2). Using normal BMI as the reference, obesity (BMI ≥ 27.5 kg/m²) was associated with a higher discrete-time hazard of incident CVD (DTHR, 3.73; 95% CI, 1.54–9.00; P = 0.003). The corresponding observed cumulative event proportions were 25.7% at 3 years and 37.1% at 5 years in the obesity category, compared with 11.0% and 17.8%, respectively, among participants with normal BMI. The estimate for overweight was elevated but imprecise (DTHR, 1.83; 95% CI, 0.77–4.35; P = 0.173), while the estimate for underweight was also highly imprecise (DTHR, 0.80; 95% CI, 0.14–4.42; P = 0.797). Because the underweight group included only 13 participants, these categorical estimates should be interpreted as supportive sensitivity findings rather than definitive evidence of category-specific effects.

Table 2
Asian BMI categories and incident cardiovascular/cerebrovascular disease.

Asian BMI category	N	3-y cumulative events	5-y cumulative events	3-y risk	5-y risk	Adjusted DTHR vs normal	P
Underweight (< 18.5)	13	1	3	7.7%	23.1%	0.80 (0.14–4.42)	0.797
Normal (18.5–22.9)	73	8	13	11.0%	17.8%	Reference	-
Overweight (23.0-27.4)	62	9	14	14.5%	22.6%	1.83 (0.77–4.35)	0.173
Obesity (> = 27.5)	35	9	13	25.7%	37.1%	3.73 (1.54-9.00)	0.003

Parsimonious Count Model

In the parsimonious model, a greater number of baseline cardiometabolic comorbidities were associated with a higher discrete-time hazard of incident CVD (Table 3 and Fig. 3). Each additional comorbidity was associated with a 55% higher estimated hazard (DTHR, 1.55; 95% CI, 1.03–2.35; P = 0.037). The functional-deficit count was not clearly associated with the outcome (DTHR, 1.12; 95% CI, 0.76–1.64; P = 0.576), nor was the treatment-indicator count (DTHR, 0.87; 95% CI, 0.62–1.23; P = 0.442). This model was prespecified as a parsimonious association analysis and should not be interpreted as a validated individual-risk prediction model.

Table 3
Discrete-time regression estimates for incident cardiovascular/cerebrovascular disease.

Exposure	Model	DTHR	95% CI	P
Age, per 10 years	Demographic core	1.45	0.99–2.14	0.058
BMI, per 5 kg/m²	Demographic core	2.19	1.31–3.66	0.003
Hypertension	Comorbidity	1.21	0.58–2.51	0.610
Diabetes	Comorbidity	1.76	0.83–3.75	0.144
Dyslipidemia	Comorbidity	1.69	0.83–3.43	0.148
ADLs deficit	Function	1.48	0.65–3.38	0.346
IADLs deficit	Function	0.78	0.40–1.53	0.472
Other function deficit	Function	1.54	0.61–3.91	0.364
Cancer medication indicator	Treatment	1.26	0.58–2.74	0.554
Surgery indicator	Treatment	0.73	0.34–1.54	0.410
Radiotherapy indicator	Treatment	0.81	0.33–1.95	0.635
Mobility severity, per point	Mobility	1.24	1.01–1.51	0.037
Comorbidity count, per condition	Parsimonious count model	1.55	1.03–2.35	0.037
Functional-deficit count, per deficit	Parsimonious count model	1.12	0.76–1.64	0.576
Treatment-indicator count, per indicator	Parsimonious count model	0.87	0.62–1.23	0.442

Discussion

In this discrete-time cohort of 183 adults with cancer who had no documented CVD at baseline, 43 incident events were observed: 27 by the 3-year assessment and 16 additional events by the 5-year assessment. The observed cumulative event proportions were 14.8% and 23.5%, respectively. Four findings were most consistent across the prespecified analyses. Continuous BMI was associated with a

higher estimated interval hazard, with a DTHR of 2.19 per 5 kg/m² (95% CI, 1.31–3.66). The Asian-category sensitivity analysis showed a DTHR of 3.73 for obesity versus normal BMI (95% CI, 1.54-9.00). Mobility severity was associated with a DTHR of 1.24 per point (95% CI, 1.01–1.51), and each additional cardiometabolic comorbidity was associated with a DTHR of 1.55 (95% CI, 1.03–2.35). Age showed a positive but less precise association, whereas individual comorbidities, ADLs/IADLs indicators, and the treatment indicators had wide CIs that included the null. These estimates describe associations within cancer survivors and should not be interpreted as the excess risk attributable to cancer compared with a cancer-free population.

Adiposity was the most consistent individual risk factor in this study. The 2022 European Society of Cardiology cardio-oncology guideline recommends systematic assessment and management of obesity and other modifiable cardiovascular risk factors during and after cancer treatment (2). BMI may act as a marker of adiposity-related cardiometabolic burden, which commonly coexists with hypertension, diabetes, dyslipidemia, and sedentary behaviors (17). This recommendation is consistent with the use of Asian-specific BMI thresholds, because cardiometabolic complications may occur at lower BMI levels in Asian populations (7). Prospective Chinese studies have also reported graded associations between body size, metabolic abnormalities, and subsequent cardiovascular or cerebrovascular outcomes (8, 9). In the present study, the concordance between the continuous BMI analysis and the categorical Asian BMI analysis supports the robustness of the direction of association. However, the categorical groups were small, and the BMI threshold analysis should be regarded as a clinically informed sensitivity analysis rather than evidence that a specific cutoff is biologically causal.

Mobility severity was associated with incident CVD, whereas the individual ADLs, IADLs, and other-function indicators were not clearly associated. This pattern is compatible with, but does not prove, a pathway in which reduced mobility captures a broader combination of low physical activity, frailty, sarcopenia, and reduced cardiopulmonary reserve. Evidence from Chinese longitudinal cohorts has linked functional limitations and functional dependence with subsequent CVD, although these studies were not restricted to cancer survivors (9, 18). Among cancer survivors, accelerometer-measured moderate-to-vigorous activity was associated with lower CVD risk in the UK Biobank (11). The differences between mobility severity and ADLs/IADLs findings may reflect differences in measurement, limited statistical power, or the fact that mobility captures a more proximal marker of reduced physical reserve. Because the present study is observational and functional status was measured at baseline, the direction of this relationship cannot be established. Nevertheless, a brief assessment of mobility and functional decline may provide useful information for survivorship risk stratification and rehabilitation referral.

The treatment indicators were not clearly associated with incident CVD in this cohort. This result should not be interpreted as evidence against treatment-related cardiovascular toxicity. The cardiovascular effects of cancer therapy vary according to treatment class, cumulative dose, timing, radiation exposure, baseline cardiovascular risk, and competing cancer-related factors (2, 19). A recent population-based study also demonstrated substantial heterogeneity in cardiovascular outcomes according to systemic

treatment exposure, with treatment-specific associations that were not uniform across heart failure, ischemic disease, and stroke outcomes (6, 20). Our treatment variables were broad indicators of medication use, surgery, and radiotherapy and did not capture specific agents, cumulative doses, treatment timing, radiation fields, or cancer stage. Therefore, they were unlikely to identify treatment-specific toxicity reliably. The imprecise estimates should be interpreted as inconclusive rather than as evidence of no treatment-related risk.

The main contribution of this study is its within-cancer risk-factor framework. Recent high-quality studies have primarily examined the overall cardiovascular burden among cancer survivors in comparison with cancer-free individuals (3, 20), cancer therapy-related cardiovascular toxicity and surveillance (6, 19), or physical activity as an individual exposure (11). This body of research has underscored the significance of cardio-oncology; however, it has not fully addressed the practical question central to this investigation: among cancer patients without pre-existing CVD at baseline, which characteristics should be prioritized in identifying individuals at heightened risk for subsequent CVD events? To address this gap, our study systematically evaluated four predefined domains within a unified analytical framework: demographic and lifestyle factors, cardiometabolic comorbidities, functional status, and cancer treatment indicators. Notably, the inclusion of BMI as a continuous variable, the examination of Asian-specific BMI categories in sensitivity analyses, and the separate evaluation of mobility severity collectively provide clinically nuanced insights that extend beyond the scope of any single treatment or lifestyle factor. Furthermore, the findings presented in this study carry important implications for preventive strategies. Recent expert recommendations published in JACC: Cardio Oncology emphasize the annual assessment and optimization of cardiovascular risk factors following cancer therapy, with enhanced surveillance for survivors identified as being at elevated risk (19). Cardiometabolic comorbidities should be comprehensively evaluated in the context of a patient's cancer history, rather than approached as isolated chronic conditions (17). During routine follow-up in oncology or primary care settings, clinicians are advised to assess BMI, blood pressure, glucose levels, lipid profiles, smoking and alcohol consumption, mobility, and functional decline. Patients presenting with elevated BMI, multiple cardiometabolic disorders, or declining mobility warrant intensified management strategies, including targeted risk factor mitigation, tailored physical activity interventions or rehabilitation programs, and cardiovascular monitoring adapted to their specific treatment history. These findings underscore the importance of integrating cardiometabolic assessments into clinical triage and preventive care planning.

These findings also have direct implications for prevention. Recent expert recommendations published in JACC: Cardio-Oncology advocate for annual evaluation and optimization of cardiovascular risk factors following cancer therapy, coupled with enhanced surveillance for survivors identified as high-risk (19). Accordingly, the concurrent assessment of cardiometabolic comorbidities and cancer history is essential to ensure a holistic and effective approach to patient care (17). In routine oncology or primary care follow-up, clinicians should assess BMI, smoking status, alcohol consumption, blood pressure, glucose levels, lipid profiles, mobility, and signs of functional decline. Patients presenting with elevated BMI, multiple cardiometabolic conditions, or deteriorating mobility may warrant more intensive management of risk factors, tailored physical activity or rehabilitation interventions, and cardiovascular

surveillance specific to their treatment history. Evidence from a large cohort of cancer survivors highlights the cardiovascular significance of objectively measured physical activity, while recent cardio-oncology guidelines underscore the importance of coordinated care between oncology and cardiovascular services (11, 19). These findings are therefore most useful for clinical triage and prevention planning. They should not be used to calculate an individual prognosis because the present model was not externally validated and was based on a limited number of events.

Several limitations should be considered. First, only 43 incident CVD events were observed, which limited statistical precision and required the use of a parsimonious, prespecified model. Accordingly, the relatively wide CIs reflect limited information, and a statistically non-significant estimate should not be interpreted as evidence that no association exists. Second, outcomes were recorded only at scheduled 3- and 5-year assessments, and exact event dates and death dates were unavailable. Although the discrete-time survival model was appropriate for the interval-based structure of the data, it could not determine the exact timing of events, estimate short-term hazard patterns, or support a formal competing-risk analysis for death. Third, information on cancer site, stage, recurrence status, treatment agent, cumulative dose, treatment timing, and radiation field was unavailable or incompletely coded. The broad treatment indicators may consequently conceal clinically important treatment-specific effects and differences in treatment intensity. Finally, although the analyses were based on clinically prespecified exposure domains and adjusted for available covariates, residual confounding from cancer severity, socioeconomic conditions, diet, medication adherence, treatment intent, and other unmeasured health behaviors remains possible. However, given the observational nature of the study and the possibility that baseline characteristics may reflect early disease burden or frailty, the findings should be interpreted as carefully adjusted associations. These results may aid in risk stratification and hypothesis generation but should not be construed as causal evidence or as confirmation that modifying any single factor would necessarily prevent CVD.

Conclusions

Among Chinese adults with cancer who were free of CVD at baseline, higher continuous BMI, obesity defined by Asian-specific thresholds, greater severity of mobility limitations, and an increased number of cardiometabolic comorbidities were associated with an elevated discrete-time risk of incident CVD during the 3- and 5-year follow-up periods. These findings underscore the importance of integrated cardiometabolic and functional surveillance in cancer survivorship. However, cautious interpretation is warranted due to the small number of observed events, interval-based outcome assessments, limited information on treatment details, and the absence of data on mortality timing. Future research involving larger cohorts with adjudicated heart and stroke outcomes, precise event dates, comprehensive cancer treatment details, repeated measurements of risk factors, and competing-risk methodologies is essential for external validation and clinical application.

Declarations

Ethics approval and consent to participate:

The study was approved by the ethics review committee (institutional review board) of Peking University. All participants granted formal written consent for their involvement.

Consent to Participate:

Not applicable.

Consent for Publication:

All authors have given final approval of the version and agreed with the publication of this study here.

Conflict of Interest Statement:

The authors declare that they have no conflict of interest.

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Author Contribution

WJL and MJ were responsible for the study concept and design. QYW and CMH extracted and collated the data. WJL and LML performed the statistical analysis and interpretation. WJL drafted the manuscript and conducted the literature search. LJ contributed to manuscript revision, supervised the research and provided critical review. All authors reviewed and approved the submitted version of the manuscript.

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Availability of data and materials

The datasets generated and/or analyzed during the current study are available in the China Health and Retirement Longitudinal Study repository [http://Charls.pku.edu. cn].

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Figures

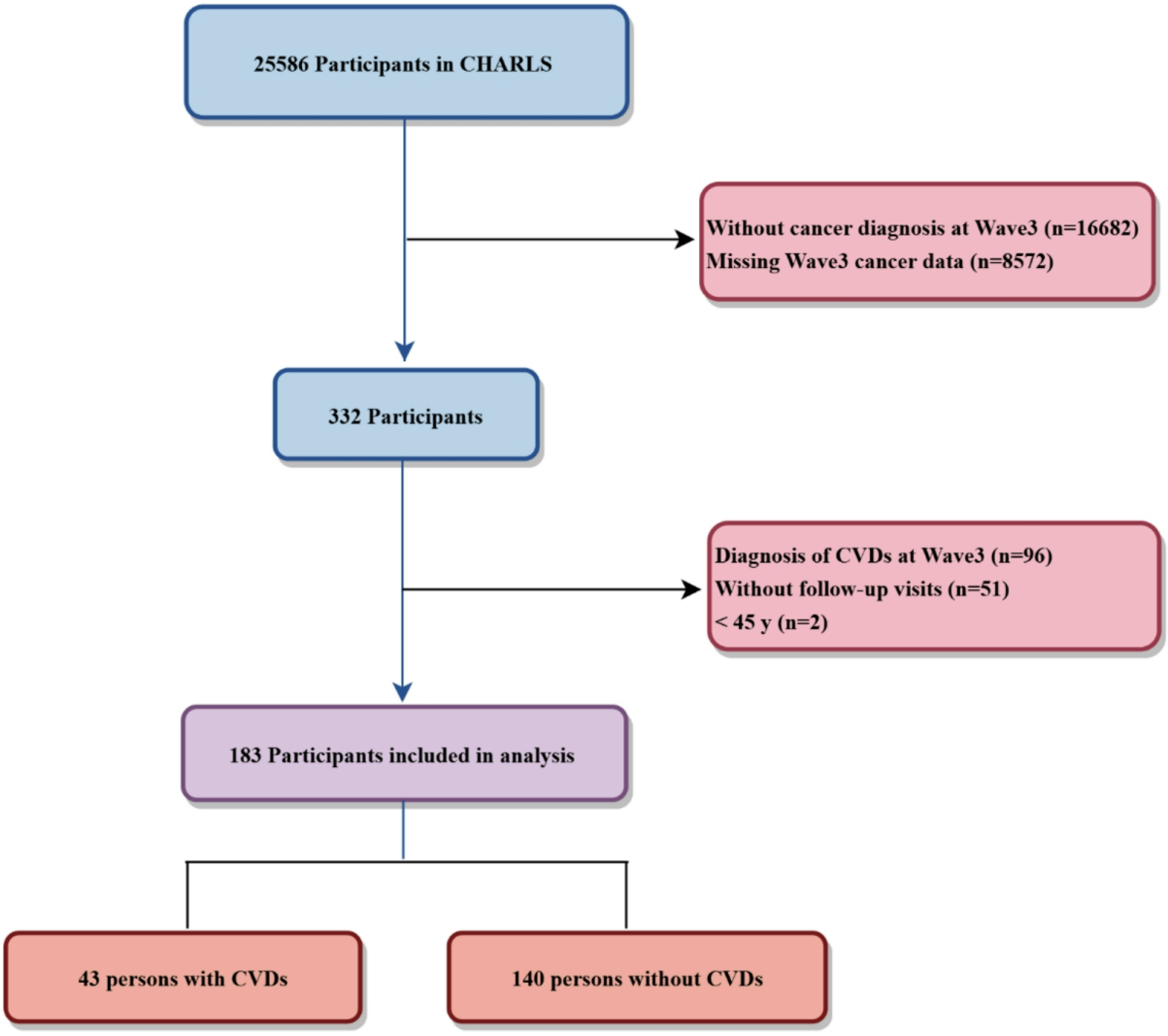


Figure 1

Flowchart of Included Participants.