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Incident Cardiovascular Diseases Among Survivors of High-Risk Stage II–III Colorectal Cancer: A Cluster-Wide Cohort Study

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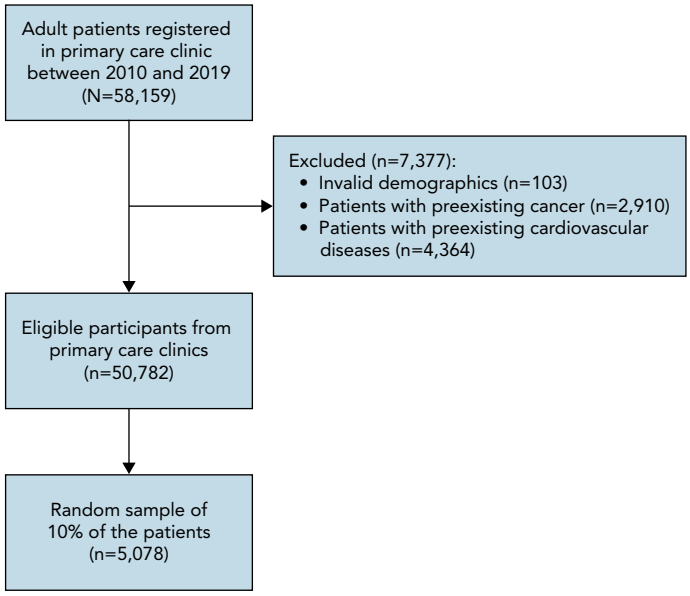
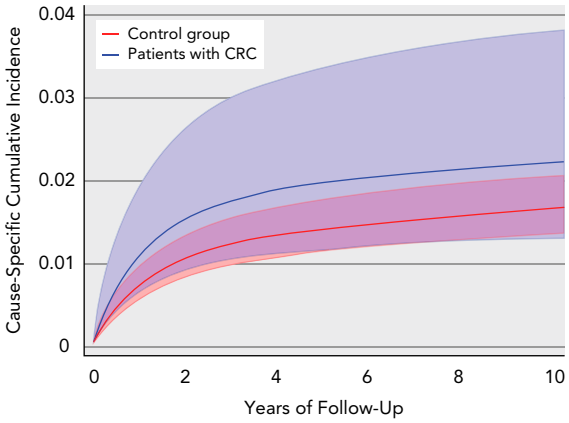
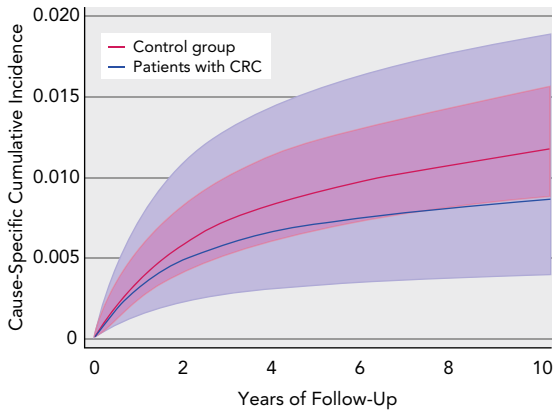


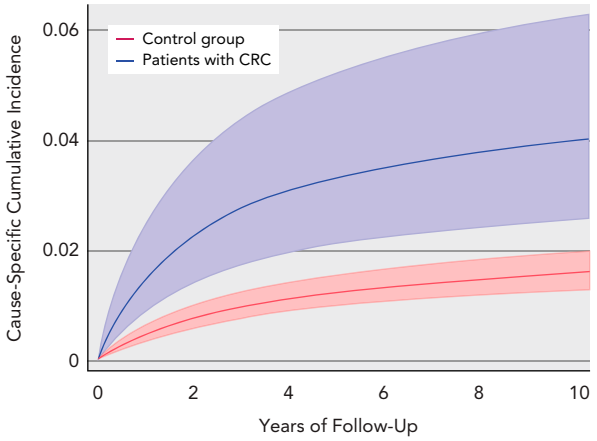
eFigure 1. Flowchart outlining the inclusion and exclusion criteria for the control group (n=5,078).



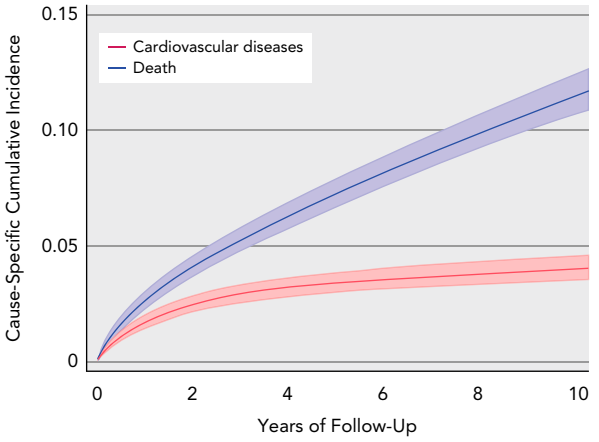
eFigure 2. Cause-specific cumulative incidences of ischemic heart disease, with death as competing risk. Bands represent 95% confidence intervals.
Abbreviation: CRC, colorectal cancer.



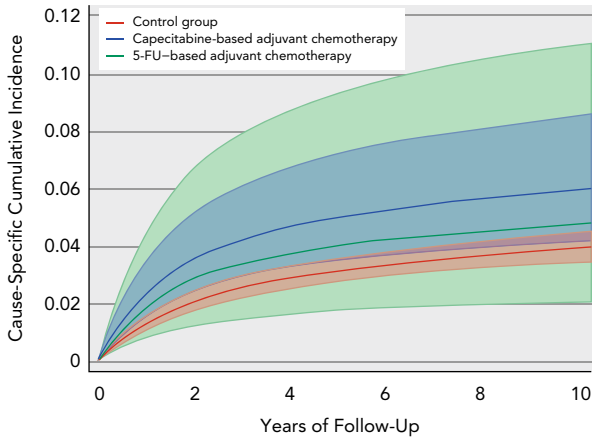
eFigure 3. Cause-specific cumulative incidences of heart failure and cardiomyopathy, with death as competing risk. Bands represent 95% confidence intervals.
Abbreviation: CRC, colorectal cancer.



eFigure 4. Cause-specific cumulative incidences of stroke, with death as competing risk. Bands represent 95% confidence intervals.
Abbreviation: CRC, colorectal cancer.



eFigure 5. Cause-specific cumulative incidence of cardiovascular diseases among the control group, with death as competing risk. Bands represent 95% confidence intervals.



eFigure 6. Cause-specific cumulative incidence of cardiovascular diseases with different adjuvant chemotherapy regimens and in control group, with death as competing risk. Bands represent 95% confidence intervals.

eTable 1. ICD-9-CM Codes of the Outcomes (Cardiovascular Diseases)

Cardiovascular Disease	ICD-9-CM Codes
Ischemic heart disease	410–413, 414.0, 414.8, 414.9, 429.7, V45.81, V45.82
Cardiomyopathy and heart failure	425, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 428, V42.1
Stroke	430–432, 433.01, 433.11, 433.21, 433.31, 433.81, 433.91, 434.01, 434.11, 434.91, 435, 436, 437.0, 437.1

eTable 2. ICD-9-CM Codes of the Medical Conditions and Associated Medications

Medical Condition	ICD-9-CM	Medications
Hypertension	401.×, 402.×, 403.×, 404.×, 405.×	Amlodipine, Diltiazem, Felodipine, Nifedipine, Verapamil, Atenolol, Bisoprolol Carvedilol, Labetalol, Metoprolol, Propranolol, Clonidine, Hydralazine, Losartan, Telmisartan, Valsartan, Bumetanide, Frusemide, Amiloride, Eplerenone, Spironolactone, Hydrochlorothiazide, Indapamide, Moduretic, Dyazide, Methyldopa, Doxazosin, Prazosin, Terazosin, Captopril, Enalapril, Lisinopril, Perindopril
Dyslipidemia	272.0, 272.1, 272.2, 272.3, 272.4	Atorvastatin, Rosuvastatin, Simvastatin, Fenofibrate, Gemfibrozil, Ezetimibe
Diabetes	249, 250.xx, 357.2, 362.0, 366.41, 648.0	Insulin Neutral, Insulin Lispro, Insulin Aspart, Insulin Human, Insulin Lispro Human, Insulin Aspart Human Analog, Insulin Detemir, Insulin Isophane Human, Insulin Degludec, Insulin Glargine, Gliclazide, Glimepiride, Glipizide, Metformin, Alogliptin, Linagliptin, Sitagliptin, Dulaglutide, Exenatide, Liraglutide, Lixisenatide, Pioglitazone, Dapagliflozin, Empagliflozin, Acarbose
Chronic obstructive pulmonary disease	491, 492, 496	Beclomethasone, Budesonide ± Formoterol, Fluticasone, Flutiform or equivalent, Relvar or equivalent, Seretide or equivalent, Trelegy or equivalent, Anoro or equivalent, Ultibro or equivalent, Spiolto or equivalent, Combivent or equivalent, Tiotropium, Ipratropium, Glycopyrronium, Indacaterol, Salbutamol, Montelukast, Roflumilast, Theophylline, Terbutaline
Smoking	V15.82	—
Alcohol-related diseases	291, 303, 305.0, 571.0, 571.1, 571.2, 571.3, 980.8, 980.9	—

eTable 3. Characteristics of CRC Survivors Who Received Different Adjuvant Chemotherapy Regimens (N=1,037)

Characteristic	Capecitabine-Based Chemotherapy n (%)	5-FU–Based Chemotherapy n (%)	*P* Value
Total, n	935	102	
Patient factors			
Age at cancer diagnosis,			.385
Median (IQR), y	62 (56–68)	61 (55–67)	
Sex			.047
Male	585 (62.6)	74 (72.6)	
Female	350 (37.4)	28 (27.4)	
RCS comorbidity score			.001
None	740 (79.1)	65 (63.7)	
1 comorbidity	170 (18.2)	30 (29.4)	
≥2 comorbidities	25 (2.7)	7 (6.9)	
Follow-up time for alive patients			.001
Median (IQR), y	5.4 (3.3–7.6)	9.0 (7.4–10.8)	
Fee waiver recipients (surrogate for lower SES)	115 (12.3)	23 (22.6)	.004
COPD or smoker	17 (1.8)	2 (2.0)	.919
Alcohol-related diseases	24 (2.6)	3 (2.9)	.822
Diabetes mellitus	112 (12.0)	22 (21.6)	.006
Hypertension	199 (21.3)	20 (19.6)	.694
Dyslipidemia/Hyperlipidemia	300 (32.1)	38 (37.3)	.290
Aspirin use	106 (11.3)	12 (11.8)	.897
β-blocker use	181 (19.4)	21 (20.6)	.766
Calcium channel blocker use	323 (34.6)	20 (19.6)	.002
ACE inhibitor use	198 (12.2)	20 (19.6)	.712
ARB use	36 (3.9)	3 (2.9)	.647
Diuretics use	657 (70.3)	60 (58.8)	.018
Statins use	295 (31.6)	38 (37.3)	.241
Treatment factors			
Chemotherapy			—
Capecitabine alone	537 (57.4)	—	
5-FU alone	—	78 (76.5)	
CAPOX	398 (42.6)	—	
FOLFOX	—	24 (23.5)	
Chemotherapy cycles, median (IQR), n	8 (5–8)	6 (2–6)	<.001
Chemotherapy dose reduction	148 (15.8)	15 (14.7)	.767

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; CAPOX, capecitabine and oxaliplatin; COPD, chronic obstructive pulmonary disease; CRC, colorectal cancer; FOLFOX, 5-FU/leucovorin/oxaliplatin; IQR, interquartile range; RCS, Royal College of Surgeons; SES, socioeconomic status.

eTable 4. Cause-Specific HRs for New-Onset CVDs by Different Adjuvant Chemotherapy Regimens With the 2-Month Landmark Period

Characteristic[a]	Unadjusted HR (95% CI)[b]	*P* Value	Adjusted HR (95% CI)[b]	*P* Value
Capecitabine-based chemotherapy vs control	1.41 (0.99–2.03)	.060	2.22 (1.42–3.45)	<.001
5-FU–based chemotherapy vs control	1.53 (0.63–3.71)	.349	1.62 (0.65–4.05)	.301
Age at cancer diagnosis (per 5-y increase)	1.27 (1.19–1.35)	<.001	1.13 (1.06–1.21)	<.001
Sex (male vs female)	1.48 (1.12–1.95)	.006	1.40 (1.06–1.86)	.019
RCS comorbidity score[c]				
1 comorbidity vs 0	1.16 (0.88–1.52)	.282	1.89 (1.37–2.62)	<.001
≥2 comorbidities vs 0	7.67 (5.67–10.38)	<.001	6.67 (4.59–9.70)	<.001
Fee waiver recipients (surrogate for lower SES)	1.58 (1.17–2.12)	.002	1.34 (0.99–1.81)	.059
Diabetes mellitus	2.16 (1.65–2.83)	<.001	1.40 (1.05–1.86)	.021
Hypertension	6.13 (4.65–8.06)	<.001	3.42 (2.48–4.70)	<.001
Dyslipidemia/Hyperlipidemia	3.20 (2.17–4.70)	<.001	2.53 (1.68–3.81)	<.001
Aspirin use	1.22 (0.93–1.61)	.157	0.92 (0.68–1.24)	.596
β-blocker use	2.27 (1.70–3.02)	<.001	1.31 (0.94–1.81)	.111
Calcium channel blocker use	2.53 (1.92–3.33)	<.001	1.02 (0.73–1.45)	.892
ACE inhibitor use	2.69 (2.03–3.56)	<.001	1.10 (0.80–1.50)	.553
ARB use	1.33 (0.62–2.82)	.461	0.76 (0.35–1.64)	.484
Diuretics use	1.87 (1.40–2.50)	<.001	0.96 (0.67–1.36)	.815
Statin use	4.23 (3.06–5.83)	<.001	—	—

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; COPD, chronic obstructive pulmonary disease; CRC, colorectal cancer; CVD, cardiovascular disease; HR, hazard ratio; RCS, Royal College of Surgeons; SES, socioeconomic status.
[a]Alcohol-related disease and COPD or smoker were not included in this analysis due to data scarcity. Due to the collinearity between dyslipidemia/hyperlipidemia and statins use, only dyslipidemia/hyperlipidemia was included in the multivariable analysis.
[b]Cause-specific HRs by competing risk analyses (ie, censoring death).
[c]Included peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, rheumatic disease, liver disease, hemiplegia/paraplegia, renal disease, AIDS/HIV infection.

eTable 5. Sensitivity Analysis by Adding CKD, PVD, and Anemia in Analysis of Cause-Specific HRs for New-Onset CVDs

Characteristic[a]	Univariable HR (95% CI)[b]	*P* Value	Multivariable HR (95% CI)[b]	*P* Value
Adjuvant chemotherapy for CRC (vs control)	1.45 (1.03–2.05)	.034	2.02 (1.33–3.08)	.001
Age at cancer diagnosis (per 5-y increase)	1.27 (1.19–1.35)	<.001	1.15 (1.08–1.23)	<.001
Sex (male vs female)	1.48 (1.12–1.95)	.006	1.40 (1.05–1.86)	.021
RCS comorbidity score[c]				
1 comorbidity vs 0	1.16 (0.88–1.52)	.282	1.82 (1.31–2.54)	<.001
≥2 comorbidities vs 0	7.67 (5.67–10.38)	<.001	5.52 (3.55–8.57)	<.001
Fee waiver recipients (surrogate for lower SES)	1.58 (1.17–2.12)	.002	1.34 (0.99–1.81)	.060
Diabetes mellitus	2.16 (1.65–2.83)	<.001	1.34 (1.01–1.78)	.045
Hypertension	6.13 (4.65–8.06)	<.001	3.14 (2.28–4.32)	<.001
Dyslipidemia/Hyperlipidemia	3.20 (2.17–4.70)	<.001	2.58 (1.71–3.90)	<.001
CKD	7.87 (5.57–11.12)	<.001	1.17 (0.76–1.80)	.487
PVD	6.15 (3.35–11.28)	<.001	1.36 (0.71–2.59)	.350
Anemia	4.08 (3.00–5.54)	<.001	1.69 (1.20–2.40)	.003
Aspirin use	1.22 (0.93–1.61)	.157	0.90 (0.66–1.21)	.475
β-blocker use	2.27 (1.70–3.02)	<.001	1.34 (0.97–1.86)	.079
Calcium channel blocker use	2.53 (1.92–3.33)	<.001	1.00 (0.70–1.41)	.982
ACE inhibitor use	2.69 (2.03–3.56)	<.001	1.02 (0.74–1.41)	.884
ARB use	1.33 (0.62–2.82)	.461	0.75 (0.35–1.63)	.470
Diuretics use	1.87 (1.40–2.50)	<.001	0.93 (0.66–1.33)	.705
Statin use	4.23 (3.06–5.83)	<.001	—	—

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CRC, colorectal cancer; CVD, cardiovascular disease; HR, hazard ratio; PVD, peripheral vascular disease; RCS, Royal College of Surgeons; SES, socioeconomic status.

[a]Alcohol-related disease and COPD or smoker were not included in this analysis due to data scarcity. Due to the collinearity between dyslipidemia/hyperlipidemia and statins use, only dyslipidemia/hyperlipidemia was included in the multivariable analysis.

[b]Cause-specific HRs by competing risk analyses (ie, censoring death).

[c]Included peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, rheumatic disease, liver disease, hemiplegia/paraplegia, renal disease, AIDS/HIV infection.

eTable 6. Sensitivity Analysis by Adding CKD, PVD, and Anemia in Analysis of Cause-Specific HRs for New-Onset CVDs Among Patients With CRC

Characteristic[a]	Unadjusted HR (95% CI)[b]	*P* Value	Adjusted HR (95% CI)[b]	*P* Value
Capecitabine-based vs 5-FU–based chemotherapy	1.10 (0.43–2.83)	.846	1.76 (0.58–5.35)	.316
Number of chemotherapy cycles (per 1 increase)	1.02 (0.89–1.17)	.749	1.00 (0.86–1.17)	.981
Chemotherapy dose reduction (yes vs no)	0.55 (0.19–1.53)	.251	0.40 (0.12–1.29)	.124
Age at cancer diagnosis (per 5-y increase)	1.53 (1.26–1.85)	<.001	1.43 (1.14–1.78)	.002
Sex (male vs female)	0.89 (0.48–1.67)	.719	0.71 (0.36–1.42)	.338
RCS comorbidity score[c]				
1 comorbidity vs 0	1.99 (1.03–3.84)	.040	1.80 (0.1–3.98)	.148
≥2 comorbidities vs 0	9.75 (4.50–21.12)	<.001	9.87 (3.27–29.77)	<.001
Fee waiver recipients (surrogate for lower SES)	1.15 (0.48–2.73)	.757	0.61 (0.22–1.67)	.339
Diabetes mellitus	3.30 (1.71–6.36)	<.001	1.53 (0.68–3.43)	.300
Hypertension	4.07 (2.20–7.50)	<.001	1.81 (0.82–4.01)	.145
Dyslipidemia/Hyperlipidemia	5.13 (2.57–10.25)	<.001	2.57 (1.15–5.75)	.022
CKD	3.75 (1.79–7.86)	<.001	1.09 (0.40–3.00)	.860
PVD	5.44 (1.68–17.66)	.005	0.60 (0.14–2.64)	.497
Anemia	1.42 (0.71–2.83)	.324	0.97 (0.46–2.08)	.947
Aspirin use	1.81 (0.83–3.92)	.133	2.64 (1.12–6.24)	.026
β-blocker use	1.62 (0.81–3.24)	.169	0.94 (0.43–2.08)	.887
Calcium channel blocker use	1.99 (1.08–3.69)	.028	0.56 (0.23–1.35)	.197
ACE inhibitor use	3.81 (2.06–7.05)	<.001	1.83 (0.81–4.12)	.146
ARB use	4.00 (1.41–11.38)	.009	1.61 (0.49–5.28)	.430
Diuretics use	1.25 (0.64–2.46)	.513	0.91 (0.39–2.12)	.826
Statin use	5.20 (2.60–10.39)	<.001	—	—

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CRC, colorectal cancer; CVD, cardiovascular disease; HR, hazard ratio; PVD, peripheral vascular disease; RCS, Royal College of Surgeons; SES, socioeconomic status.

[a]Alcohol-related disease and COPD or smoker were not included in this analysis due to data scarcity. Due to the collinearity between dyslipidemia/hyperlipidemia and statins use, only dyslipidemia/hyperlipidemia was included in the multivariable analysis.

[b]Cause-specific HRs by competing risk analyses (ie, censoring death).

[c]Included peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, rheumatic disease, liver disease, hemiplegia/paraplegia, renal disease, AIDS/HIV infection.

eAppendix 1. Clinical Data Analysis and Reporting System

Clinical Data Analysis and Reporting System (CDARS) is an electronic healthcare database operated by the Hospital Authority of Hong Kong, which is the sole public healthcare provider in Hong Kong. It covers approximately 90% of all secondary and tertiary care and serves a population of 7.5 million.[1,2] Patient data, including demographics, diagnoses, hospital admission and clinic attendance, treatments, laboratory results, and causes and dates of death, are recorded in the CDARS. Clinicians provide the ICD-9-CM codes for each episode of clinic attendance and hospital admission, respectively.[3,4] These codes have showed a high accuracy in diagnosing myocardial infarction and stroke with positive predictive values of 85% and 91%, respectively, in a previous study.[5] Another study also demonstrated the reliability of the CDARS in capturing the demographics and the use of antidiabetic medications with a near-perfect level of data completeness exceeding 99%.[4] High-quality population-based studies on cardiovascular diseases, oncology, and medications have been published based on information retrieved from the CDARS.[6–10]

References

1. Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. BMJ 2003;327:557–560.
2. The Government of the Hong Kong Special Administrative Region: Census and Statistics Department. Population 2020. Accessed August 8, 2020. Available at: https://www.censtatd.gov.hk/hkstat/sub/so20.jsp
3. Fung V, Cheung NT, Szeto K, et al. Hospital Authority clinical vocabulary table: the past, the present, and the future. Accessed June 1, 2022. Available at: https://bok.ahima.org/doc
4. Wong MC, Jiang JY, Tang JL, et al. Health services research in the public healthcare system in Hong Kong: an analysis of over 1 million antihypertensive prescriptions between 2004-2007 as an example of the potential and pitfalls of using routinely collected electronic patient data. BMC Health Serv Res 2008;8:138.
5. Wong AYS, Root A, Douglas IJ, et al. Cardiovascular outcomes associated with use of clarithromycin: population based study. BMJ 2016;352:h6926.
6. Chan EW, Lau WC, Leung WK, et al. Prevention of dabigatran-related gastrointestinal bleeding with gastroprotective agents: a population-based study. Gastroenterology 2015;149:586–95.e3.
7. Cheung KS, Chan EW, Wong AYS, et al. Long-term proton pump inhibitors and risk of gastric cancer development after treatment for Helicobacter pylori: a population-based study. Gut 2018;67:28–35.
8. Lau WC, Chan EW, Cheung CL, et al. Association between dabigatran vs warfarin and risk of osteoporotic fractures among patients with nonvalvular atrial fibrillation. JAMA 2017;317:1151–1158.
9. Wong AY, Root A, Douglas IJ, et al. Cardiovascular outcomes associated with use of clarithromycin: population based study. BMJ 2016;352:h6926.
10. Lee SF, Luque-Fernandez MA, Chen YH, et al. Doxorubicin and subsequent risk of cardiovascular diseases among survivors of diffuse large B-cell lymphoma in Hong Kong. Blood Adv 2020;4:5107–5117.

eAppendix 2. Royal College of Surgeons Adaptation of the Charlson Comorbidity Index

Comorbidities before colorectal cancer were measured using the Royal College of Surgeons (RCS) adaptation of the Charlson comorbidity index.[1] Cardiovascular risk factors were removed from the overall RCS score to avoid multicollinearity in regression analysis. The remaining comorbidities in the index, including peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, rheumatic disease, liver disease, hemiplegia/paraplegia, renal disease, and AIDS/HIV infection, were combined into the score.

Reference

1. Brusselaers N, Lagergren J. The Charlson comorbidity index in registry-based research. Methods Inf Med 2017;56:401–406.

eAppendix 3. Statistical Analysis Using Flexible Parametric Competing Risk Modeling Framework

The follow-up times for cardiovascular diseases (CVDs) continued until the first diagnosis of a CVD event, cancer recurrence, noncardiac death, or censor date, whichever was earlier. We censored patients who remained alive and had not developed CVD or cancer recurrence by the end of follow-up on October 31, 2021. Follow-up started after the date of the last adjuvant chemotherapy dose. We only counted the events if the diagnosis of CVD occurred beyond a landmark period of 2 months after the date of operation because most patients would have recovered from the operation and started adjuvant treatment by that time.

We evaluated the cause-specific cumulative incidence (csCI) of CVD with adjuvant chemotherapy using a flexible parametric competing risk modeling framework. We derived the csCI after adjusting for age, sex, need for medical fee waiver (surrogate of socioeconomic status), preexisting cardiovascular risk factors (chronic obstructive pulmonary disease or smoking, alcohol-related diseases, atrial fibrillation, hypertension, hyperlipidemia, dyslipidemia, diabetes mellitus, and depression) (see supplemental eTable 2), and Royal College of Surgeons (RCS) comorbidity score, which were established or theoretical risk factors for CVD.

We presented the csCIs plots of CVD for the patients who received adjuvant chemotherapy and the comparison group. As secondary analyses, we included the csCI plots of each CVD endpoints (ie, ischemic heart disease, heart failure and cardiomyopathy, and stroke) for both groups. We also presented the csCI of CVD for patients exposed to different adjuvant chemotherapy regimens. Furthermore, we computed the ratios of predicted cumulative incidence of CVD, colorectal cancer relapse, and cancer-specific death among patients at 5 and 10 years and computed their respective 95% confidence intervals by bootstrapping with 1,000 resamplings. Finally, we performed sensitivity analyses to test whether the results were robust with respect to the absence of a landmark period, and to adjust for additional cardiovascular risk factors (chronic kidney disease, peripheral vascular disease, and anemia) in addition to the RCS comorbidity score.

References

1. Gichangi A, Vach W. The analysis of competing risks data: a guided tour. Stat Med 2005;132.
2. Pintilie M. Competing Risks: A Practical Perspective. Hoboken, NJ: John Wiley & Sons Ltd.; 2006.
3. Gray RJ. A class of K-sample tests for comparing the cumulative incidence of a competing risk. Ann Stat 1988;16:1141–1154.
4. Andersen PK, Geskus RB, de Witte T, et al. Competing risks in epidemiology: possibilities and pitfalls. Int J Epidemiol 2012;41:861–870.
5. Geskus RB. Data Analysis with Competing Risks and Intermediate States. Boca Raton, FL: CRC Press; 2016.
6. Kipourou DK, Charvat H, Rachet B, et al. Estimation of the adjusted cause-specific cumulative probability using flexible regression models for the cause-specific hazards. Stat Med 2019;38:3896–3910.
7. Lambert P. Standardized cumulative incidence functions. Accessed March 5, 2020. Available at: https://pclambert.net/software/standsurv/standardized_cif/
8. Armitage P, Berry G, Matthews JNS. Statistical Methods in Medical Research, 4th ed. Oxford, UK: Blackwell Science Ltd.; 2002.
9. Yusuf S, Joseph P, Rangarajan S, et al. Modifiable risk factors, cardiovascular disease, and mortality in 155722 individuals from 21 high-income, middle-income, and low-income countries (PURE): a prospective cohort study. Lancet 2020;395:795–808.
10. Nguyen HN, Fujiyoshi A, Abbott RD, et al. Epidemiology of cardiovascular risk factors in Asian countries. Circ J 2013;77:2851–2859.