

Long-term cardiac morbidity in adolescent and young adult survivors of classical Hodgkin lymphoma: the British Columbia experience

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Supplementary Table 1: Chronic Disease Registry (CDR) definitions for diagnosis

Condition	Definition	ICD 9/10 Code
Chronic Obstructive Pulmonary Disease	One hospitalization or two physician visits in one year, with ICD code(s) specified.	J41 Simple and mucopurulent chronic bronchitis; J42 Unspecified chronic bronchitis; J43 Emphysema; J44 Other chronic obstructive pulmonary disease; 491 Chronic bronchitis; 492 Emphysema; 496 Chronic airways obstruction, not elsewhere classified
Diabetes Mellitus	One hospitalization or two physician visits in one year with diagnostic code(s) specified below; or two or more insulin prescriptions in one year; or two	E10 Type 1 diabetes mellitus; E11 Type 2 diabetes mellitus; E13 Other specified diabetes mellitus; E14 Unspecified diabetes mellitus; 250 Diabetes mellitus Gestational

	or more oral antihyperglycemic (not including metformin) prescriptions in one year; or one insulin and one oral antihyperglycemic (including metformin) in one year; or 2 metformin prescriptions and 1 physician visit in one year with ICD code(s) specified. Cases of suspected gestational diabetes in women aged 10-54 are not included by excluding hospitalizations, physician claims or prescriptions within the time period 120 days preceding or 180 days after hospital records containing birth-related diagnostic codes.	
Heart Failure	One hospitalization or two physician visits in one year with diagnostic code(s) specified.	I50 Heart Failure; 428 Heart Failure
Hypertension	One hospitalization or two physician visits in one year with diagnostic code(s) specified.	I10 Essential (primary) hypertension; I11 Hypertensive heart disease; I12 Hypertensive renal disease; I13 Hypertensive heart and renal disease; I15 Secondary hypertension; 401 Essential hypertension; 402 Hypertensive heart disease; 403 Hypertensive renal disease; 404

		Hypertensive heart and renal disease; 405 Secondary hypertension
Ischemic Heart Disease	Two physician visits with Angina ICD-9 code 413 plus one prescription (as specified in drug list) in one year; or one specialist visit with Angina ICD-9 code 413 plus one prescription (as specified in drug list) in one year; or two physician visits with two ICD9 410, 411, 412, 413, 414 in one year; or 1 CABG,PCI/PCTA procedure code specified; or one hospitalization with any IHD code specified.	I20 Angina pectoris; I21 Acute myocardial infarction; I22 Subsequent myocardial infarction; I23 Certain current complications following acute myocardial infarction; I24 Other acute ischaemic heart diseases; I25 Chronic ischaemic heart disease; 410 Acute myocardial infarction; 411 Other acute and subacute forms of ischaemic heart disease; 412 Old myocardial infarction; 413 Angina pectoris; 414 Other forms of chronic ischaemic heart disease; CCI/CCP Procedure Code Description 1IJ57LA Extraction, coronary arteries using open approach; 1IJ57VS Extraction, coronary arteries using open approach with placement/implant of stent; 1IJ76 Bypass, coronary arteries (endoscopic or open approach); 1U50 Dilation, coronary artery; 1IJ57G Extraction, coronary arteries using percutaneous transluminal arterial approach; 48.11 Aortocoronary Bypass For Heart Revascularization, Unqualified; 48.12 Aortocoronary Bypass Of One Coronary Artery; 48.13 Aortocoronary Bypass Of Two Coronary

		Arteries; 48.14 Aortocoronary Bypass Of Three Coronary Arteries; 48.15 Aortocoronary Bypass Of Four Or More Coronary Arteries; 48.16 Single (Internal) Mammary-Coronary Artery Bypass; 48.17 Double (Internal) Mammary-Coronary Artery Bypass; 48.19 Single (Internal) Mammary-Coronary Artery Bypass; 48.02 Percutaneous Transluminal Coronary Angioplasty Without Mention; 48.03 Percutaneous Transluminal Coronary Angioplasty With Thrombolytic
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Supplemental Table 2: 20-year cumulative incidence of heart failure and ischemic heart disease in 2-year survivors of classic Hodgkin lymphoma relative to age-, sex- and region-matched controls

	Combined CVD		HF		IHD	
	20-y cumulative incidence	95% CI	20-y cumulative incidence	95% CI	20-y cumulative incidence	95% CI
Controls	3.2%	2.7-3.7%	0.8%	0.05-0.1%	2.8%	2.4-3.3%
All cases	10.1%	7.2-12.9%	4.3%	2.3-6.2%	8.3%	5.6-11.0%
Mediastinal RT						
Yes	12.0%	7.8-16.2%	5.4%	2.4-8.3%	10.7%	6.7-14.7%
No	8.5%	4.6-12.5%	3.3%	0.8-5.8%	6.0%	2.5-9.4%
Anthracycline dose						
RT Yes, A <300	11.5%	6.4-16.7%	4.3%	1.1-7.5%	9.9%	5.0-14.7%
RT Yes, A ≥300	11.4%	4.6-18.3%	8.3%	1.4-15.3%	10.8%	4.0-17.5%

RT No, A <300	7.0%	1.5-12.4%	3.4%	0-7.5%	3.6%	0-7.3%
RT No, A ≥300	10.9%	4.5-17.2%	3.6%	0-7.3%	8.8%	2.7-14.9%
Stage						
Limited	7.4%	3.5-11.4%	2.0%	0.3-3.8%	6.7%	2.9-10.6%
Advanced	11.3%	7.5-15.1%	5.2%	2.4-8.0%	9.2%	5.7-12.8%
Age at Diagnosis						
<30 y	5.5%	2.9-8.0%	2.6%	0.7-4.5%	4.4%	2.1-6.7%
≥30 y	18.5%	12.1-24.8%	7.4%	3.1-11.6%	15.3%	9.3-21.4%
Sex						
Male	15.1%	10.4-19.7%	5.9%	2.7-9.2%	13.1%	8.6-17.6%
Female	4.6%	1.7-7.4%	2.5%	0.6-4.5%	2.9%	0.5-5.3%

Supplementary Table 3: Multi-regression analysis of relative risk of heart failure (HF) and ischemic heart disease (IHD) in adolescent and young adult survivors with classical Hodgkin lymphoma treated with upfront therapy only versus age-, sex- and region-matched population controls

	HF			IHD		
	RR	95% CI	p-value	RR	95% CI	p-value
Radiation and anthracycline <300 mg/m2	4.95	1.86 - 13.16	0.001	3.03	1.67 - 5.47	<0.001
Radiation and anthracycline ≥ 300 mg/m2	4.63	1.12 - 19.21	0.035	2.53	1.02 - 6.30	0.045
No radiation and anthracycline <300 mg/m2	3.01	0.68 - 13.25	0.146	1.63	0.64 - 4.16	0.305

No radiation and anthracycline $\geq$ 300 mg/m²	3.75	1.26 - 11.11	0.017	0.25	0.03 - 1.78	0.166
Male	1.60	0.90 - 2.85	0.111	2.23	1.59 - 3.12	<0.001
Advanced stage	1.09	0.60 - 1.98	0.776	0.96	0.69 - 1.32	0.785
Era of Treatment After January 1, 2005	1.18	0.48 - 2.87	0.721	1.02	0.62 - 1.70	0.932
Age >30 y at diagnosis	3.27	1.77 - 6.05	<0.001	2.08	1.52 - 2.86	<0.001
Diabetes	5.36	2.67 - 10.76	<0.001	2.55	1.54 - 4.24	<0.001
Hypertension	2.44	1.22 - 4.89	0.012	2.58	1.68 - 3.97	<0.001
COPD	4.67	1.82 - 11.97	0.001	0.65	0.15 - 2.76	0.558