A Clinical Prediction Model of Asymptomatic Left Ventricular Dysfunction in Survivors of Childhood Cancer in Ontario, Canada

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Background

- Survivors of childhood cancer (CCS) treated with anthracyclines or radiation have a higher risk of cardiomyopathy (CMP), like asymptomatic left ventricular dysfunction (ALVD) and heart failure (HF).
- Current guidelines recommend a risk-stratified schedule of screening. However, CCS may benefit from personalized prognostic screening for early intervention.
- A clinical prediction model which identifies CCS at high risk for ALVD can be used to determine different thresholds for continued screening. This may support precise decision-making to improve the health outcomes of CCS.

Objectives

- To develop a dynamic prediction model of ALVD risk using individual-level data in Ontario, Canada.
- To assess the impact of ejection fraction (EF) percentage on predicting ALVD risk

Methods

Data Sources: Retrospective chart data from the Princess Margaret Cancer Centre in Ontario

Eligibility Criteria: CCS treated with anthracyclines or radiation between 0-20 years who received at least two echocardiograms between 1980/01/01 to 2022/05/31

Outcome: ALVD, defined by ejection fraction (EF) < 51% (males); < 53% (females)

Time Horizon of Predictions: Two-year risk (prediction window) over 20 years (landmark time horizon)

Model: Landmark analysis with a multivariable Cox proportional hazards model

Assessments of Model Performance: Calibration plots; time-varying AUC scores

Table 1. List of predictors for each prediction model

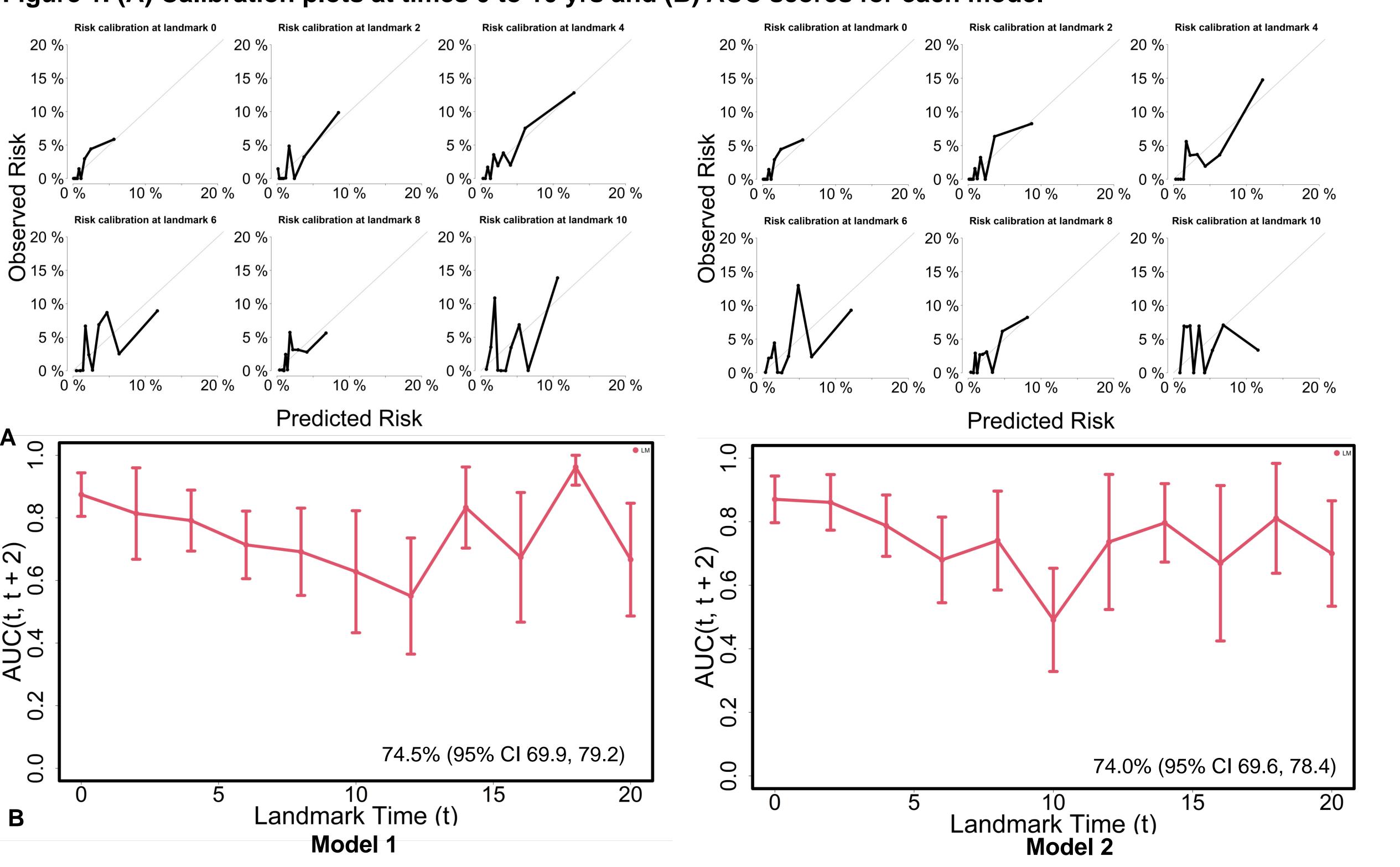| Model 1	Model 2
Age	Age
Age at diagnosis	Age at diagnosis
Time between diagnosis and 1st screening	Time between diagnosis and 1st screening
Time between screening and LM	Time between screening and LM
No. of past screenings	No. of past screenings
CMP risk high (vs not high)	CMP risk high (vs not high)
EF percentage	**Baseline EF**
Linear interactions with LM	Linear interactions with LM
Quadratic interactions with LM	Quadratic interactions with LM

CMP = cardiomyopathy; EF = ejection fraction; LM = landmark time; Y = Yes; N = No

Results

Table 2. Number of participants and events for each model

	Model 1: EF	Model 2: Baseline EF
N participants	691	691
N events	94	99

EF = ejection fraction

Table 3. Sample characteristics

		CMP Risk (%)	
Mean age at diagnosis (Range)	7.44 (3 – 20)		
Mean attained age (Range)	31.11 (19 - 67)		
Sex: Female (%)	341 (49.4)	High	402 (58.2)
Treatment Exposure (%)			
Anthracycline	651 (94.2)	Moderate	189 (27.4)
Radiation	354 (51.2)	Low	100 (14.5)

CMP = cardiomyopathy

Figure 1. (A) Calibration plots at times 0 to 10 yrs and (B) AUC scores for each model

Model 1

Model 2

74.5% (95% CI 69.9, 79.2)

74.0% (95% CI 69.6, 78.4)

Conclusion

This prediction model demonstrated high predictive performance of ALVD in CCS using standard clinical parameters. Both models perform similarly. The models may be used for precise medical decision-making in survivors of cancer. The time-varying hazard ratios generated will be used in the microsimulation-based cost-utility analysis for routine echocardiographic screening in survivors in Canada.