Machine-extractable Markers in Chest Radiograph to Predict Cardiovascular Risk in Screening Population

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Background and Motivation

Recent studies using deep learning-based AI models on chest radiographs have shown promise in assessing biological aging and cardiovascular disease (CVD) risk[1,2]. However, the lack of explainability in these algorithms limits their clinical utility, especially in primary care where clear patient communication is crucial. This study aims to identify and test machine-extracted quantitative measurements and features from chest radiographs to predict CVD risk in screening population.

Cohort and Outcomes

Dataset/Cohort: The publicly available multicentre Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial Dataset was selected for analysis.

Eligibility Criteria: Chest radiograph taken within 1 year of baseline questionnaire; Age 55-75; **No prior stroke, coronary heart disease, heart attack or cancer** before the first chest radiograph.

Survival end-points: Two survival end-points, CVD mortality and 10-year major adverse cardiovascular events (MACE) were extracted from the dataset.

Chest Radiograph Quality Check & Processing

As quantitative measurements are sensitive to orientation and rotation of the image, a quality check algorithm based on segmentation was developed to assess patient rotation, adequacy of inspiration and lung coverage. Cases that do not have full lung coverage in the image, or are rotated, or have abnormal spine curvature are excluded from the study.

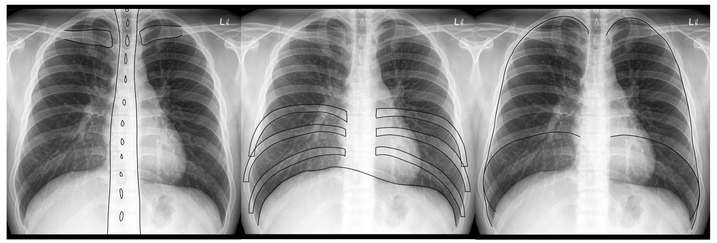


Figure 2. Example of structural segmentation mask used for assessing patient rotation, adequacy of inspiration and lung coverage.

Feature Extraction

Expanding on the well established cardiothoracic ratio, several quantitative measurements aimed at characterising cardiomediastinal geometry, aortic knuckle calcification and descending aorta tortuosity were developed and extracted by using the structure segmentation model. The transverse thoracic diameter was measured at three different levels for normalization of the extracted features. The degree of aortic knuckle calcification was also assessed by measuring the circumferential coverage around the aortic knuckle.

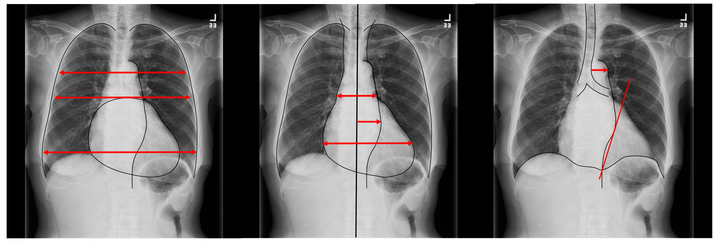


Figure 1. Example of reference transverse thoracic diameters, and quantitative imaging features characterising cardiomediastinal geometry and aorta tortuosity.

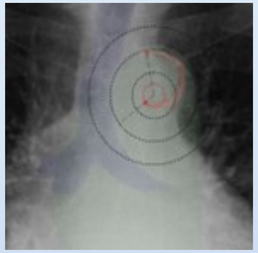
Analysis & Results

Modelling: The association between the imaging features, clinical characteristics (age, sex, BMI, smoking status, hypertension, diabetes, liver disease) and the two survival end-points was analysed by using proportional hazard regression, with feature selection done by LASSO.

A total of **29,453 subjects** from 10 independent centres met the eligibility and quality check criteria and were used for analysis (median follow-up time 19 years). **A total of 32 imaging features** were extracted and analysed. Subjects from the largest single centre (n=5693) were used for fitting of all models, which were then used to evaluate subjects from the other 9 centres.

Evaluation: Concordance Index (C-Index) and Area Under Receiver Operating Characteristic Curve (AUROC) were used to evaluate the prognostic performance of the each of the Cox models for CVD mortality and 10-year MACE respectively. Prognostic performance of the models were also compared with two state-of-the-art deep learning-based models from the literature.

Analysis & Results



Measurement of aortic knuckle calcification coverage.

Table 1. Prognostic performance of different models that use different combination of features, and comparison with state-of-the-art deep learning-based models.

	CVD Mortality C-Index (95th CI)	10Y MACE AUROC (95th CI)
Incidents / total number of samples	*2455/23760*	*1720/12289*
Image features + age + sex	0.74 (0.73 – 0.75)	0.72 (0.70 – 0.74)
Clinical characteristics	0.75 (0.74 – 0.76)	0.72 (0.70 – 0.75)
Image features + Clinical characteristics	0.76 (0.75 – 0.77)	0.73 (0.71 – 0.76)
CXR CV-RISK[2]	0.73 (0.72 – 0.74)	0.71 (0.69 – 0.73)
Chronological Xp-Age[1]	0.67 (0.66 – 0.68)	0.65 (0.63 – 0.66)
CXR CV-RISK[2] + Clinical characteristics	0.77 (0.72 – 0.74)	0.74 (0.71 – 0.76)
Chronological Xp-Age[1] + Clinical characteristics	0.74 (0.75 – 0.75)	0.71 (0.69 – 0.73)

Table 2. Adjusted (Age, Sex, Smoking, Co-morbidity) hazard ratio of Imaging features used in the model.

Imaging Features		PLCO Discovery Cohort (N = 5693, 437 incidents)		PLCO Validation Cohort (N = 23760, 2455 incidents)	
	SD (% or Ratio)	Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value
Aortic calcification coverage†	6.96	1.12 (1.05 – 1.12)	<0.000	1.09 (1.06 – 1.12)	<0.000
Mediastinal width at aortic valve level*†	3.72	1.40 (1.27 - 1.54)	<0.000	1.28 (1.22 – 1.33)	<0.000
Maximal descending aorta lateral displacement*†	2.99	1.34 (1.22 – 1.46)	<0.000	1.19 (1.14 – 1.23)	<0.000
Right cardiac diameter*†	3.42	1.15 (1.05 – 1.26)	0.003	1.08 (1.04 – 1.12)	0.0001
Aortic Knuckle Width*	1.62	1.24 (1.13 – 1.37)	<0.000	1.14 (1.09 – 1.79)	<0.000
Cardiothoracic ratio	3.73	1.21 (1.02 – 1.24)	0.0148	1.09 (1.04 – 1.13)	0.0001

* Features normalised by transverse thoracic diameter at the aortic knuckle level.
† Features used in the multivariable Cox model.

Summary & Applications

This study demonstrated the performance of several simple measurements on the chest radiograph that can be extracted by machine in predicting CVD mortality and MACE in asymptomatic screening population, with performance comparable to that of state-of-the-art black box type deep learning-based models. This approach to AI based CVD risk assessment preserves model explainability which we believe is a critical element in fostering confidence and adoption.

The abundance and widespread use of chest radiographs in hospitals and clinics makes it a potential effective opportunistic screening tool for assessing CVD risk without incurring extra cost associated with lab-test used in traditional cardiovascular risk assessment. The simplicity and accessibility of digital chest radiographic images can facilitate retrospective or real-time monitoring of CVD risk across diverse populations.

Conflict of Interest: RD, YCH & ET are shareholders and/or employees of Detect Medical Technology Limited, a Hong Kong start-up focused on providing AI/ML, software and medical imaging analysis services. No conflict of interests declared for all other authors.

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References:

1. Mitsuyama, Yasuhito et al. Chest radiography as a biomarker of ageing: artificial intelligence-based, multi-institutional model development and validation in Japan. *The Lancet Healthy Longevity*.

2.Weiss J et al. Deep learning to estimate cardiovascular risk from chest radiographs: A risk prediction study. *Ann Intern Med*.

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