Mammography—an opportunity to optimise women's heart health?

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Barraclough and colleagues[1] are to be congratulated on their paper published in *Heart*. The authors report on the work of a diverse team of clinicians, imaging scientists and bioinformaticians to discover and validate a machine learning algorithm to predict cardiovascular events from routine mammograms. Mammographic features, such as breast arterial calcification and tissue density, have previously been recognised as associated with the risk of cardiovascular disease. However, Barraclough *et al*[1] have taken a novel approach to progress this further. They have applied machine learning approaches to mammograms from the 49 196 women in the Lifepool cohort with linked hospitalisation and death outcome data. This modelling benefited from a median follow-up of 8.8 years, and a substantial number of first major cardiovascular events. Using a deep learning model, and only mammography features and participant age, the team were able to predict cardiovascular events with a similar performance to complex risk algorithms, such as the America Heart Association PREVENT (Predicting Risk of Cardiovascular Disease Events) equation.

While the performance of the mammography plus age based model of Barraclough *et al*[1] did not exceed that of models with an extensive number of clinical variables, there are substantial pragmatic benefits to a simple measure that does not require additional history or blood tests and can potentially occur in a manner integrated into a routine breast screening visit. Of interest, the addition of more complex clinical variables in a combined model, including blood test results, improved performance only slightly. This is pragmatically important. Generation of data for risk scores such as PREVENT represents a substantial resource "cost" (eg, blood test) and "time" (including additional clinical history taking, and clinical measurements of blood pressure). Opportunistically using mammography data represents little direct cost and perhaps avoids the risk of "losing the moment" of a woman's interaction with the health system at breast screening.

Our current efforts to reduce coronary artery disease (CAD) events by identifying and treating standard modifiable risk factors (hypertension, dyslipidaemia, diabetes mellitus and smoking) are effective at reducing heart attack and stroke at a population level, but morbidity and mortality related to cardiovascular disease remain high. This is particularly true in women and younger adults, where risk algorithms underperform.

Compounding the suboptimal performance of traditional risk factor algorithms in women is poor awareness. There is a substantial under-appreciation of heart disease as a threat to women by both women and the health system. In contrast with what is commonly thought, breast cancer causes only about 10% of the total deaths globally compared with those resulting from cardiovascular disease.[2] The awareness and concern regarding breast cancer is reflected in high uptake rates in screening programmes (>67% in the US and UK).[1] Mammography may therefore represent a "touch point" for raising awareness about cardiovascular risk and disease in women and, as illustrated by Barraclough *et al*[1], may also provide powerful prognostic information regarding future cardiovascular events with prediction rates similar to those obtained using traditional risk factors.

Future work should explore which components of major adverse cardiovascular events are best predicted by mammographic data. Do mammographic data predict heart failure, stroke or atherosclerotic CAD events better? While the authors show strong prognostic use of the machine learning algorithm, like much data driven modelling, there is uncertainty about the potential mechanism or mechanisms that are reflected by the machine learning model. Does this reflect vascular health and systemic susceptibility to atherosclerosis, or different hormonal or metabolic profiles of the individual? It may be possible in future work to explore this further, perhaps in cohorts with both CT coronary angiography data and mammography data.

Breast screening provides an interesting contrast to screening for cardiovascular risk and disease. Oncologists would not consider treating a patient for breast cancer (with surgery or chemotherapy) based only on their risk factors or even their mammography findings. Ultrasound and biopsy would follow. In the case of CAD and myocardial infarction risk, we now have the ability to image the underlying disease itself. Improved technology allows non-invasive imaging of coronary atherosclerosis with clinically available CT coronary angiography, with an extremely strong correlation with the gold standard intravascular imaging.[3] Indeed, in contrast with mammography for breast cancer detection, there are effectively no differential diagnoses for plaque visualised on CT in the coronary artery. Measures of non-calcified plaque volume more directly reflect the vulnerable plaque and appear to have even greater prognostic value, with a recent study showing that individuals with >85 mm^3 of non-calcified plaque volume had a >40% rate of major adverse cardiovascular events over 5 years.[4] It appears that it is time to consider a multi-step approach to prevention of heart attacks, which would enable more rapid translation of tools, such as the mammography machine learning algorithm of Barraclough *et al*.[1]

One of the challenges with new tools that show promise for improved cardiovascular risk assessment remains implementation. Barraclough and colleagues[1] acknowledge this and suggest the value of a prospective implementation trial with health economic evaluation to establish clinical utility, acceptability and cost effectiveness of mammography based cardiovascular risk prediction. However, it is not clear what this would entail, and what the next steps might be. Would patients and treating physicians be guided to assess and treat traditional risk factors with primary prevention guidelines or, particularly given the prognostic value of this score without the need for knowing the patient's risk factors, would it be more appropriate to triage patients for CT coronary angiography? A potential clinical pathway is shown in figure 1. The application of a new risk tool to triage individuals for screening for subclinical CAD is particularly relevant with the increasing emphasis on atherosclerotic CAD as the disease itself,[5] and heart attacks as more of a catastrophic endpoint. Prospective implementation studies can then be assessed for their ability to reduce the number needed to scan to detect clinically actionable CAD.[6]

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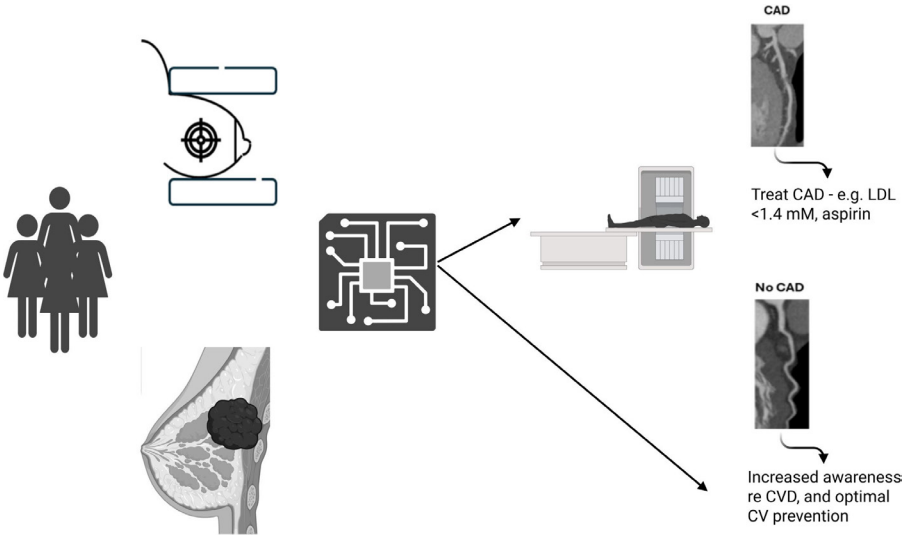

Figure 1 Potential clinical pathway for implementation. CAD, coronary artery disease; CV, cardiovascular; CVD, cardiovascular disease; LDL, low density lipoprotein.

This paper has come at a time of frustration regarding the suboptimal performance of traditional risk factor algorithms for risk assessment and preventative strategies in women. Further validation and prospective implementation studies of the mammography machine learning algorithm of Barraclough *et al*[1] would be valuable.

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