Echocardiographic age and sex estimation using artificial intelligence predicts overall survival

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**Background:** Transthoracic echocardiography (TTE) is increasingly used by point-of-care ultrasound (POCUS) devices. Age and sex can be estimated by artificial intelligence (AI) based on various sources. The current study aimed to test whether deep learning (DL) networks could be trained to predict a patient's age and sex using a TTE. We hypothesized that DL-predicted age would be superior to chronological age in predicting long-term survival.

**Methods:** The analysis was based on 122,014 unique patients who underwent TTE evaluation between 2007 and 2021 at large tertiary medical center. Survival data were available for all subjects from the National Population Register. Three mutually exclusive cohorts were used for training (N=76,342 [62%]), validation (N=22,825 [19%]) and testing (N=22,847 [19%]). A fourth cohort (N=650), from a different hospital, was used for external validation. The testing cohort was used to evaluate the accuracy in estimating age and sex. The cohort was divided into two mutually exclusive groups; (1) the patients whose machine-estimated age was ≥ 5 years of their chronological age (20% of the cohort), (2) all other patients. A multivariate Cox regression model was used to investigate the association between age estimation and chronological age with overall survival.

**Results:** The final test cohort included 18,447 unique patients, of whom 10,640 (58%) were men with a median age of 66 (IQR 54-76). The machine learning model was able to estimate age with an average error of 4.9 years, a Root Mean Square Error (RMSE) of 6.3 and a Pearson correlation coefficient (r) of 0.922. Sex was estimated as a probabilistic value with total accuracy of 96.1% and an area under the curve (AUC) of 0.993. Consistent results were obtained with external validation from a different hospital (RMSE = 7.04, r=0.897 and an AUC of 0.988). During a median follow-up of 4.3 (IQR, 2.1-6.3) years, 5147 (27.9%) patients died. A multivariate Cox regression model with adjustment for age, sex, and ejection fraction demonstrated that age prediction ≥ 5 years of chronological age was associated with an independent and significant 48% increased risk of death during follow-up (95% CI 1.38-1.59, p<0.001). When machine’s age prediction was used as a continuous variable in the same model, each year above the chronological age was associated with an independent and significant 8% increased risk of death (95% CI 1.05-1.10, p<0.001). Similarly, a higher probability of male sex among female subjects was also associated with a significant 63% increased risk of death in the same model (95% CI 1.38-1.92, p<0.001).

**Conclusions:** Applying AI to the standard TTE allows the prediction of a patient's sex and estimation of age. Machine-based estimation is an independent predictor of overall survival and, with further evaluation, can be used for risk stratification and estimation of biological age at the point of care.
Kaplan-Meier survival curve by delta-age \( \geq 5 \) adjusted to chronological age

\[
\text{HR}=1.48 \\
P<0.001
\]

Number at risk

\[
\begin{array}{cccccccc}
\text{Delta-age} < 5 & 16808 & 15316 & 13582 & 11524 & 9624 & 8004 \\
\text{Delta-age} \geq 5 & 4152 & 3778 & 3389 & 2909 & 2436 & 2056 \\
\end{array}
\]

Kaplan-Meier survival curve by sex prediction adjusted to chronological age (females predicted as males)

\[
\text{HR}=1.63 \\
P<0.001
\]

Number at risk

\[
\begin{array}{cccccccc}
\text{Same} & 8348 & 7607 & 6736 & 5733 & 4823 & 4038 \\
\text{Female as Male} & 399 & 354 & 297 & 253 & 207 & 182 \\
\end{array}
\]