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RESEARCH LETTER

Deep learning-enabled echocardiographic assessment of biventricular ejection fractions: the dual-task QUEST-EF model

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Introduction

Rapid and accurate assessment of left and right ventricular (LV and RV) systolic function is essential in contemporary cardiology practice. Although 2D echocardiography (2DE) remains the most commonly used imaging modality for this task, it has inherent limitations: it requires multiple views to appropriately assess LV ejection fraction (LVEF) and does not enable the quantification of RV ejection fraction (RVEF). 3D echocardiography (3DE) offers clear incremental value over 2DE.[1,2] However, recent surveys have revealed that 3DE is still underutilized for assessing ventricular volumes and ejection fractions, most commonly due to the lack of dedicated training, time constraints, and the complexity of post-processing, in addition to the limited availability of 3DE probes and software packages and challenges posed by poor acoustic windows.[3,4]

Previously, we developed and externally validated a deep learning (DL)-based, segmentation-free tool to predict RVEF from a single 2D apical four-chamber view (A4C) echocardiographic video, which demonstrated diagnostic and prognostic utility comparable with 3DE and cardiac magnetic resonance imaging.[5] In the present study, we built upon this work and aimed to develop QUEST-EF (**QU**antification of **E**chocardiographic **ST**udies—**E**jection **F**raction), a dual-task DL model for predicting both 3DE-derived LVEF and RVEF based on a single A4C video. Additionally, we sought to test QUEST-EF across a diverse spectrum of acquired and congenital cardiac diseases and various geographic regions.

Methods

QUEST-EF is a complex end-to-end DL pipeline comprising two main components. The first component is responsible for preprocessing the input DICOM file through several steps, such as converting its frames to grey-scale, generating a binary mask denoting the region of interest, cropping the frames and resizing them to 192 × 192 pixels, applying min–max scaling, and sampling 16 frames from each cardiac cycle. Additionally, this component includes a view classifier to ensure that only A4C videos are passed to the next pipeline component, an orientation classifier that enables the horizontal flipping of videos recorded in the Stanford orientation, and a transformer we previously trained as proposed by Reynaud *et al.*[6] to identify end-systolic frames, which are then used to split the videos into cardiac cycles without relying on an electrocardiographic signal. The second component comprises two video vision transformers (ViViT-b 16 × 2), which were first pre-trained on 29 876 unlabelled A4C videos from 15 661 echocardiographic studies in a self-supervised fashion as described previously.[7] In the subsequent supervised training phase, one of the transformers was trained for predicting LVEF on the publicly available EchoNet-Dynamic dataset comprising 10 030 A4C videos with 2DE-derived labels (only LVEF) and a dual-centre 3DE dataset comprising 5341 A4C videos with 3DE-derived labels (both LVEF and RVEF), whereas the other transformer was trained for predicting RVEF only on the latter dataset.

Beyond testing QUEST-EF internally on 20% of the dual-centre dataset (i.e. the internal test set), its performance was also evaluated in a labelled external test set, which included (i) 238 A4C videos of 238 patients with mixed cardiac diseases from an Italian centre of whom 187 had available data regarding heart failure hospitalizations and all-cause mortality during follow-up, (ii) 177 A4C videos of 90 adults with congenital heart disease from a British centre, (iii) 183 A4C videos (with LVEF labels only) of 183 patients with mixed cardiac diseases from a German centre, (iv) 20 A4C videos (with RVEF labels only) of 20 patients with severe tricuspid regurgitation from another German centre, and (v) 4695 A4C videos of 901 healthy adults enrolled in the World Alliance of Societies of Echocardiography study (*Figure 1*). Last, the associations between the predictions and 10-year all-cause mortality were also investigated in a Hungarian, low-risk, community-based cohort (1166 unlabelled A4C videos of 1166 individuals).

Performance metrics are reported at the study level. The source code of QUEST-EF is available on GitHub (https://github.com/szadam96/quest-ef),

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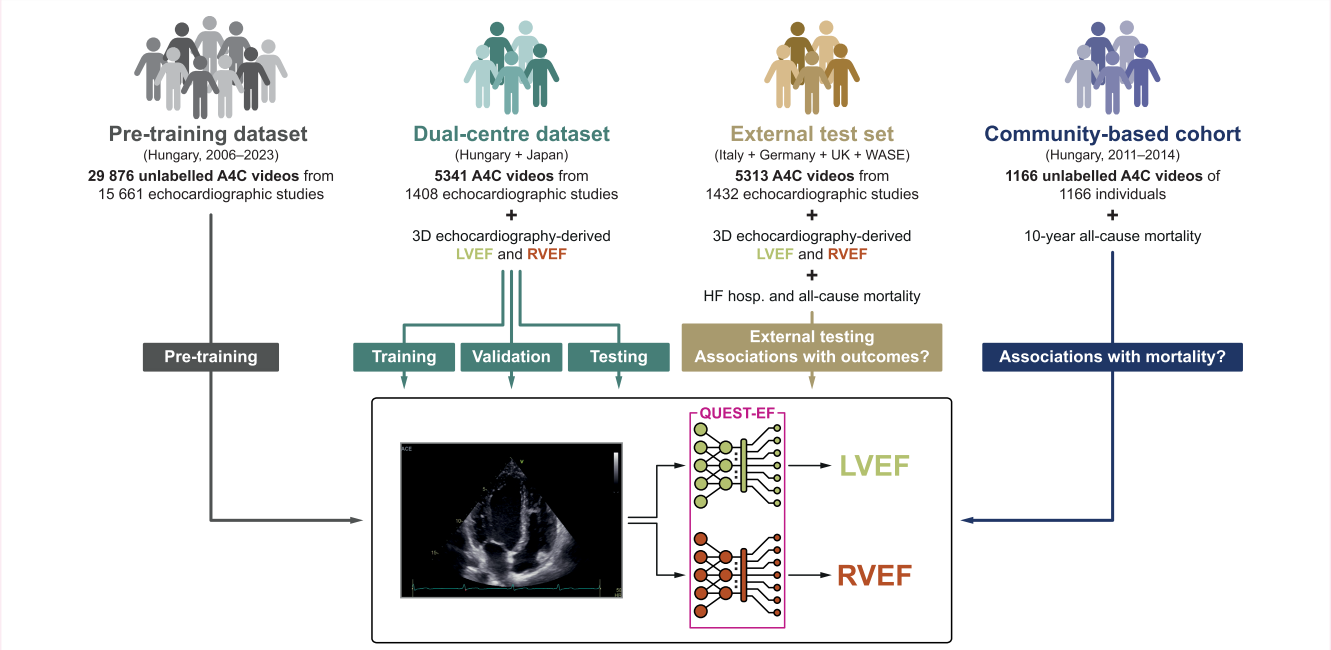

Figure 1 Training and testing datasets used for the development and testing of QUEST-EF. A4C, apical four-chamber view; hosp., hospitalization; LVEF, left ventricular ejection fraction; RVEF, right ventricular ejection fraction; WASE, World Alliance of Societies of Echocardiography.

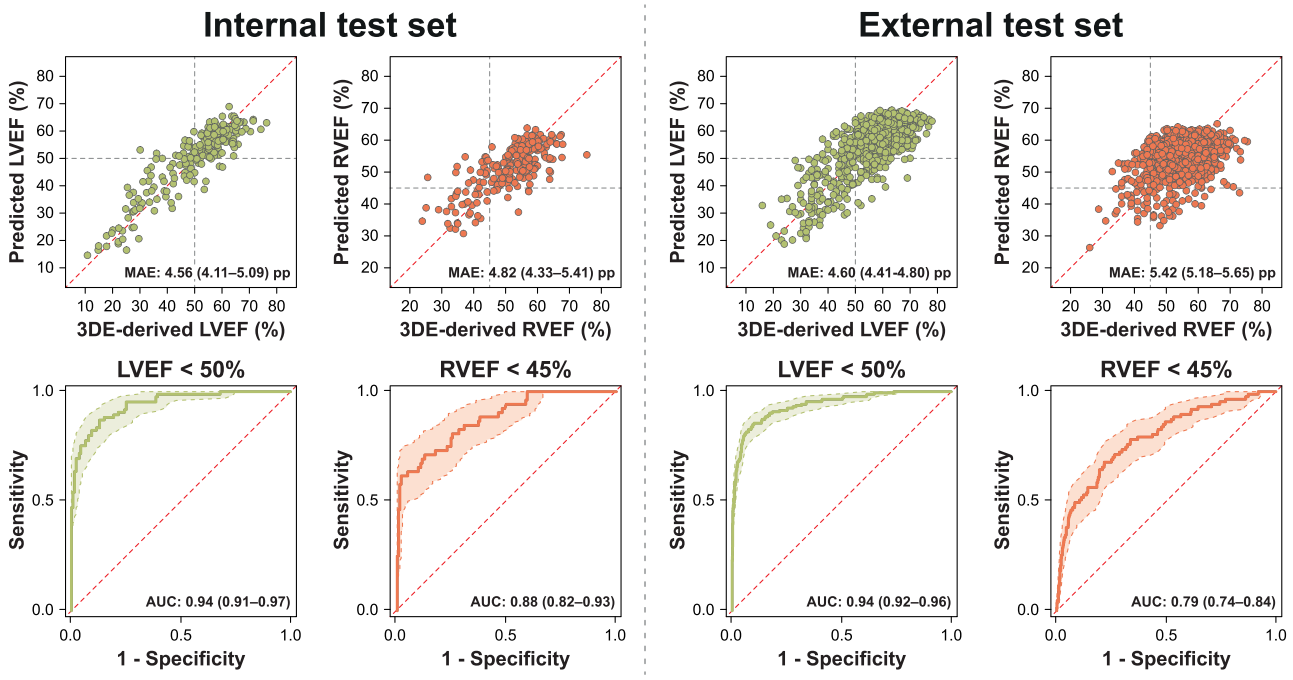

Figure 2 Performance of QUEST-EF. The internal test set for predicting LVEF included 822 A4C videos [LVEF < 50%: 322 (39.2%) videos] from 225 studies [LVEF < 50%: 85 (37.8%) studies], whereas the test set for predicting RVEF comprised 825 A4C videos [RVEF < 45%: 196 (23.8%) videos] from 219 studies [RVEF < 45%: 52 (23.7%) studies]. The external test set for predicting LVEF included 5293 A4C videos [LVEF < 50%: 212 (4.0%) videos] of 1412 patients [LVEF < 50%: 174 (12.3%) patients], whereas the test set for predicting RVEF comprised 5130 A4C videos [RVEF < 45%: 210 (4.1%) videos] of 1249 patients [RVEF < 45%: 87 (7.0%) patients]. The performance of QUEST-EF is reported at the study level (i.e. by averaging the predictions of all A4C videos acquired during the same echocardiographic study). 95% confidence intervals and bands were calculated from 10 000 stratified bootstrap resamples. 3DE, three-dimensional echocardiography; A4C, apical four-chamber view; AUC, area under the receiver operating characteristic curve; LVEF, left ventricular ejection fraction; MAE, mean absolute error; pp, percentage point; RVEF, right ventricular ejection fraction.

ensuring transparency and reproducibility. The study protocol conforms with the principles outlined in the Declaration of Helsinki and was approved by the ethics committees of the institutions participating in this study.

Results

During internal and external testing, QUEST-EF predicted LVEF with mean absolute errors (MAEs) of 4.56 [95% confidence interval (CI): 4.11–5.09] and 4.60 (95% CI: 4.41–4.80) percentage points, respectively, and RVEF with MAEs of 4.82 (95% CI: 4.33–5.41) and 5.42 (95% CI: 5.18–5.65) percentage points (*Figure 2*). In the internal test set, the model identified LV and RV systolic dysfunction (i.e. LVEF < 50% and RVEF < 45%) with areas under the receiver operating characteristic curve (AUCs) of 0.94 (95% CI: 0.91–0.97) and 0.88 (95% CI: 0.82–0.93), respectively, whereas, in the labelled external test set, it achieved AUCs of 0.94 (95% CI: 0.92–0.96) and 0.79 (95% CI: 0.74–0.84) in these tasks (*Figure 2*). Among the 187 patients with available outcome data [28 (15.0%) died or were hospitalized due to heart failure during the median follow-up duration of 1.1 (interquartile range: 0.5–1.6) years], the QUEST-EF-predicted EF values were associated with the composite endpoint of all-cause death and heart failure hospitalization [LVEF—adjusted hazard ratio (aHR): 0.945 (95% CI: 0.913–0.979), $P = 0.002$; RVEF—aHR: 0.927 (95% CI: 0.877–0.979), $P = 0.006$], independent of age and sex. In the community-based cohort [10-year all-cause mortality rate: 131/1166 (11.2%)], the predictions were also associated with all-cause mortality [LVEF—aHR: 0.947 (95% CI: 0.924–0.970), $P < 0.001$; RVEF—aHR, 0.877 (95% CI: 0.845–0.909), $P < 0.001$], independent of the Framingham Risk Score and LV filling pressures estimated by E/e′ ratio.

Discussion

LVEF and RVEF are the most important non-invasive surrogates of systolic cardiac function, serving as strong determinants of symptoms, functional capacity, quality of life, and clinical outcomes. To support clinicians in the echocardiographic assessment of these parameters, we developed QUEST-EF, a vendor-independent and segmentation-free DL-based solution capable of accurately predicting biventricular EFs using a single, routinely acquired A4C video. While designing QUEST-EF, we intentionally chose a segmentation-free approach to enable the model to extract both direct and indirect indicators of ventricular function from all visualized anatomical structures rather than restricting it to outlining and tracking the endocardial border of the ventricles. This approach is particularly relevant for predicting RVEF, as contouring the RV in a single plane would only yield RV fractional area change that has shown significant disagreements with 3DE-derived RVEF.[8] Moreover, not relying on accurate endocardial border tracking ensures that the model's performance is less likely to degrade if some LV or RV myocardial segments are visualized poorly or fall outside the imaging sector.

Another key strength of QUEST-EF is its end-to-end design, which enables the rapid and simultaneous prediction of LVEF and RVEF from a single echocardiographic video without requiring manual intervention. The use of transformers instead of spatiotemporal convolutional neural networks represents another technical advancement over our previously published single-task model,[5] as well as the employment of a state-of-the-art pretraining technique that leveraged a large, unlabelled dataset to enhance performance in the downstream task of predicting LVEF and RVEF.[7] We believe these technical innovations collectively contributed to the robust performance of QUEST-EF that we observed across a wide range of acquired and congenital cardiac diseases at centres spanning six continents. Although we should be very cautious when comparing performance metrics calculated in different datasets, the performance of QUEST-EF falls within a similar range to that reported for other recently published DL models,[5,9,10] further supporting its robustness.

We recognized the importance of providing users with a ready-to-use tool. To achieve this, in addition to publishing the source code of QUEST-EF, we developed an intuitive web interface for the model (http://quest-ef.com/) to facilitate further testing and allow free use for research purposes.

We foresee that QUEST-EF could be particularly valuable in clinical scenarios where 3D imaging is not feasible or available—such as point-of-care ultrasound examinations performed by non-cardiologist users, including internal medicine specialists, pulmonologists, cardiac surgeons, intensivists, and emergency physicians—by enabling fast, automated, and accurate screening for LV and RV dysfunction.

Despite its robustness, QUEST-EF has a few limitations that should be acknowledged. First, it is currently intended for research use only and has not been approved for clinical application. Therefore, regulatory approval and further rigorous testing are required before it can be integrated into clinical decision-making. Second, QUEST-EF has higher prediction errors and a larger generalization gap for RVEF than for LVEF, most likely due to the RV's more complex geometry and contraction pattern, which make single-view assessment of its function more challenging than that of the LV. However, in our previous work with a single-task model,[5] we demonstrated that a similarly segmentation-free approach could still achieve higher sensitivity than expert human readers, implying that it may be particularly well suited for screening purposes by non-expert physicians. Last, we may assume that a model analysing multiple views would achieve even better performance than our single-view model, particularly for RVEF prediction. Nevertheless, we deliberately opted for this more simplistic approach, which requires only a single routinely acquired echocardiographic view, to facilitate QUEST-EF's future clinical adoption and integration into handheld ultrasound devices and ensure ease of use, even for physicians with limited expertise in echocardiography.

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Conflict of interest: Á. Szijártó, Á. Szeier, and B. Magyar are employees of Argus Cognitive, Inc. and receive financial compensation for their work (unrelated to the content of the present manuscript). A.C. has received educational grants, personal fees, and non-financial support from Janssen-Cilag, Ltd. (unrelated to the content of the present manuscript). B.K.L. and A.F. report personal fees from Argus Cognitive, Inc. (unrelated to the content of the present manuscript). E.S. has received personal fees from GE Healthcare and 123sonography and is an employee and a shareholder of AstraZeneca (all unrelated to the content of the present manuscript). M. Takeuchi has received grants from Philips Medical Systems (unrelated to the content of the present manuscript). B. Merkely has received grants from Boston Scientific and Medtronic and personal fees from Biotronic, Abbott, AstraZeneca, Novartis, and Boehringer Ingelheim (all unrelated to the content of the present manuscript). R.M.L. is in the

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Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

Appendix

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