Appendix 1 Model development

The 10-second, 12-lead ECG data at a frequency of 500 Hz were converted into a 5,000 × 12 matrix. A Butterworth bandpass filter with a cut-off frequency range of 1-40 Hz was applied to all ECG signals.

We developed a multi-attention convolutional neural network (MANet) that leverages the ResNet-18 backbone with one-dimensional residual convolutional blocks (15). The MANet incorporates both local and global spatial attention mechanisms to fuse information from 12-lead ECG data to detect high-risk echocardiographic features. The MANet consists of four residual layers, each fused with a squeeze and excitation channel attention (SE Block) to form the SE-BasicBlock (31). The initial convolutional block uses a kernel size of 15 to extract a wider range of input signal features, whereas the SE-BasicBlock utilizes a convolution with a kernel size of three to capture intricate local signal features. SE-BasicBlock is composed of a series of convolutional blocks, rectified linear unit (ReLU) activations, batch normalization (BN) layers, and SE blocks. Skip connections were introduced to address issues related to gradient vanishing and explosions. The input dimensions for each layer of the backbone are {5,000, 1,250, 1,250, 625, 313, and 157} and the channel sizes are {12, 64, 64,128, 256, and 512}. Therefore, the final convolutional layer output a matrix size of 512 × 157 pixels. This matrix is then passed through an adaptive global pooling layer to generate a global vector *g* with a size of 512 × 1. AttBlock was designed to generate attention maps based on global feature *g* for local feature maps f1, f2, and f3 at different scales for different layers of the network to highlight the saliency regions (32). Subsequently, the global attention-weighted local features (weighted-f1, weighted-f2, and weighted-f3) of various scales are merged and fed into the transformer encoder (33) to further incorporate the spatial global context, where the input features have dimensions of 512 with eight attention heads and two layers. Finally, a linear layer and sigmoid activation function were employed for binary classification, ranging from zero to one.

The training process involved feeding ECGs into the network, utilizing binary cross-entropy loss as the loss function, and optimization using the Stochastic Gradient Descent (SGD) optimizer with a learning rate of 0.001. After each epoch, the network was tested using a validation set. The best model was selected based on the lowest loss function values in the validation set. All codes were implemented using the PyTorch 1.13.1 framework and Python 3.7.13.

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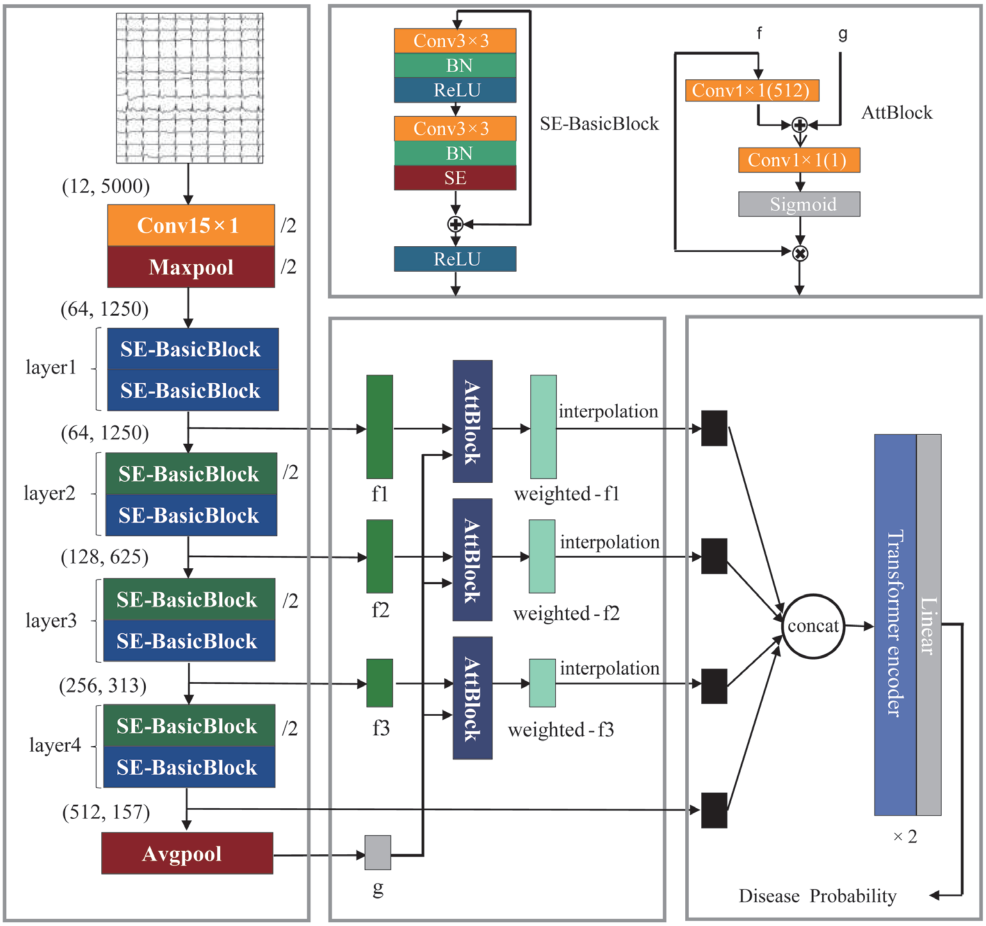

Figure S1 Architecture of MANet. This diagram illustrates the whole architecture of the MANet. Conv, convolution; SE, squeeze and excitation channel attention; BN, batch normalization; ReLU, rectified linear unit.

Table S1 Model performance for high-risk echocardiographic features in testing and external validation sets using 12-lead and single-lead ECG

ECG leads	Cohort	AUROC (95% CI)	AUPRC (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Accuracy (95% CI)
12 leads	Internal testing	0.81 (0.76-0.86)	0.54 (0.45-0.64)	0.80 (0.71-0.87)	0.76 (0.71-0.80)	0.47 (0.42-0.52)	0.93 (0.91-0.95)	0.77 (0.74-0.80)
	External validation	0.80 (0.72-0.87)	0.54 (0.41-0.67)	0.71 (0.52-0.86)	0.76 (0.69-0.83)	0.40 (0.31-0.49)	0.92 (0.87-0.95)	0.75 (0.68-0.83)
I lead	Internal testing	0.73 (0.67-0.78)	0.39 (0.33-0.46)	0.74 (0.65-0.82)	0.54 (0.49-0.59)	0.30 (0.27-0.33)	0.89 (0.85-0.92)	0.58 (0.54-0.63)
	External validation	0.74 (0.65-0.82)	0.43 (0.26-0.59)	0.65 (0.45-0.82)	0.69 (0.61-0.77)	0.32 (0.24-0.40)	0.90 (0.84-0.93)	0.68 (0.62-0.75)

ECG, electrocardiogram; AUROC, area under the receiver operating characteristic curve; AUPRC, area under the precision-recall curve; CI, confidence interval.

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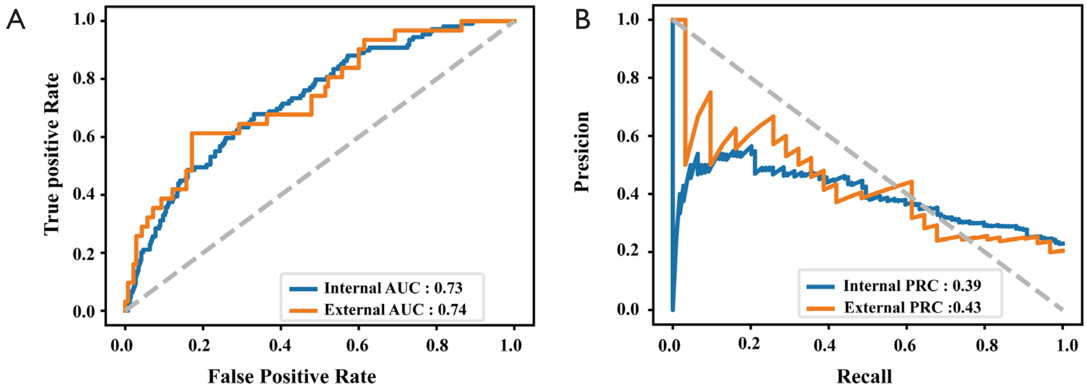

Figure S2 Model performance in high-risk echocardiographic features using single-lead ECG. (A) The AUROC of MANet for identifying high-risk echocardiographic features in HCM is shown for the testing and external validation sets. (B) The AUPRC of MANet for identifying high-risk echocardiographic features in HCM is shown for the testing and external validation sets. AUC, area under the curve; PRC, precision-recall curve; ECG, electrocardiogram; AUROC, area under the receiver operating characteristic curve; HCM, hypertrophic cardiomyopathy; AUPRC, area under the precision-recall curve.

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