Classifying Early Stage Cardiac Amyloid from Echocardiogram Images Using Deep Learning

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Introduction
Cardiac amyloidosis is characterized by the extracellular deposition of misfolded protein aggregates. The accumulation of these insoluble fibrils results in the disruption of normal tissue structure and function. Patients with cardiac involvement with the light chain (AL) form of amyloidosis have a median survival of less than six months without treatment. At the later stages of cardiac amyloidosis, there is significant ventricular wall thickening and abnormal diastolic function that may alert clinicians to the diagnosis. However, these significant structure changes are associated with high morbidity and mortality which compel clinicians to develop tools for earlier diagnosis.

Hypothesis
A machine learning technique known as deep learning, e.g., Deep Convolutional Neural Networks (CNNs), has potential to explore and discover latent imaging features that are difficult to categorize by the human visual system and thus be used in a development of novel algorithm to detect cardiac amyloidosis at an earlier stage of disease using 2D echocardiographic images.

Methods
A number of 800 2D echocardiographic still images from 100 patients were selected experienced cardiologists, all of which had their ground truth status (Amyloid or Control) through clinical diagnosis using a combination of echocardiographic appearance, quantitative analysis, and/or biopsy. These status data were used as the reference standard for the automated classification system. The 2D echocardiographic images were divided into data of two views at two time points in the cardiac cycle; apical 4 chamber (AP4) and parasternal long axis (PLAX) at end systole (ES) and end diastole (ED). Data was prepared by first removing the background items, e.g., patient information, miscellaneous text, or EKG rhythm strip. Then the processed images were separated into training (80%) validation (10%) and testing (10%) data for training our machine learning model. Care was taken to group images from the same patient to avoid data from the same patient appearing in both training and testing sets. Each of the views of 2D images were used directly as input to two different pretrained deep learning models (ResNet50 and VGG19) to fully explore the potential imaging features. The proposed model consisted of a base of pretrained models, dropout layers, and regularization layers to prevent model overfitting. Saliency maps of activation layers were also shown to examine the features learned from the model.

Results
A result of 75.8%, 69.2%, 70.2%, 79% in views of AP4ED, AP4ES, PLAXES, PLAXED were achieved in the views of 2D echocardiographic images.

Conclusion
We have demonstrated the feasibility of binary classification of early stage cardiac amyloidosis vs control using a deep learning architecture. Larger unannotated (without sonographer measurement lines and grids), multiple view datasets will be needed to refine performance and the learned imaging features required for examination.

Statement of Impact
There is great potential for the application of deep learning methods as an aid to cardiologists in the efficient and accurate analysis of medical images.

Keywords
deep learning, Image classification, echocardiographic images, cardiac amyloid