Deep learning augmented ECG analysis for screening and genotype prediction of congenital long QT syndrome

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Background

- Congenital long QT syndrome (LQTS) is a cardiac ion channelopathy associated with syncope, polymorphic VT, and rarely, sudden arrhythmic death. Patients may have a normal/borderline QT interval on resting ECG (concealed LQTS).
- We aimed to develop a machine learning model that could detect LQTS on baseline ECGs, even in cases where the LQTS is concealed.

Methods

- 1104 ECGs collected from 604 patients (age 38±19, female 56.4%) with clinical suspicion for an inherited arrhythmia; 74 ECGs were excluded for poor quality.
- The LQTS cohort consisted of probands and their phenotype-negative relatives identified to have a pathogenic/likely-pathogenic variant in KCNQ1 (LQT1) or KCNH2 (LQT2) genes.
- A neural network (LQTSnet) was used to discriminate between LQTS type 1, type 2, and negative genotype status from 12-lead ECGs.

Figure 1. Flow chart of patients included in the study

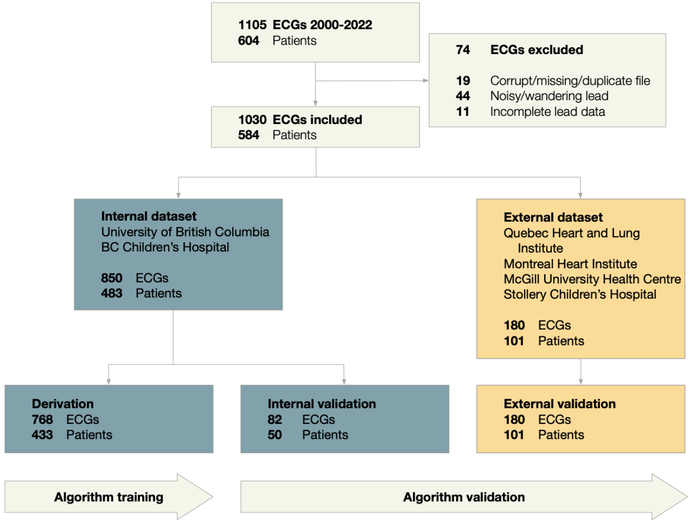

Figure 2. Model architecture for LQTSnet

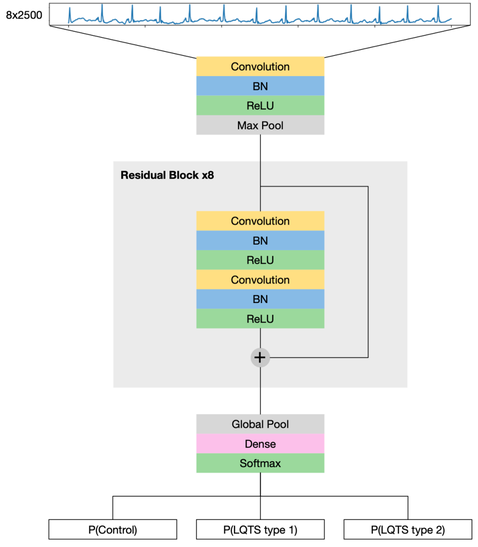

Figure 3. Detection of LQTS, (a) Internal (b) External validation

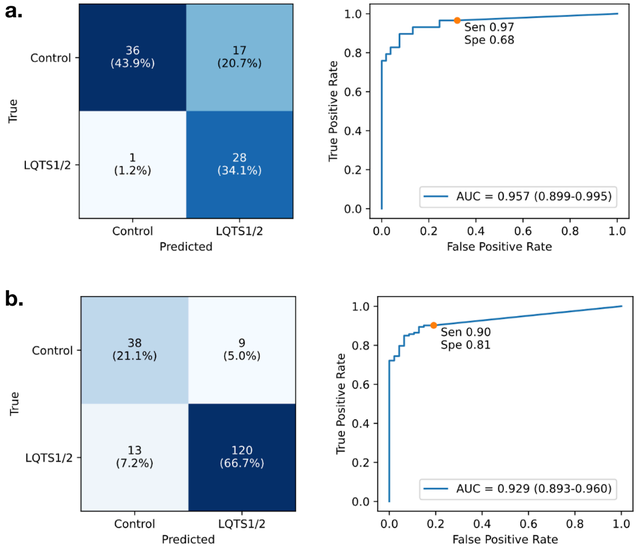

Table 1. Detection of LQTS vs. experts

	N	AUC (95% CI)	F1 score (95% CI)	Sensitivity (95% CI)
Internal validation, all ECGs				
CNN	31	0.920 (0.794-1.000)	0.786 (0.571-1.000)	0.846 (0.667-0.963)
Expert measured long QTc ◊◊	31	NA	0.214 (0.000-0.429)	0.353 (0.000-0.600)
Internal validation, normal/borderline QTc ◊				
CNN	27	0.888 (0.718-1.000)	0.700 (0.400-1.000)	0.778 (0.533-0.947)
Expert measured long QTc ◊◊	27	NA	0	0
External validation, all ECGs				
CNN	118	0.914 (0.862-0.957)	0.829 (0.744-0.902)	0.895 (0.838-0.938)
Expert measured long QTc ◊◊	118	NA	0.220 (0.134-0.305)	0.356 (0.234-0.473)
External validation, normal/borderline QTc ◊				
CNN	97	0.894 (0.833-0.947)	0.774 (0.661-0.871)	0.865 (0.792-0.924)
Expert measured long QTc ◊◊	97	NA	0	0

◊ Normal QTc if <450 ms (men) or <460 ms (women); Borderline QTc if 450-469 ms (men) or 460-479 ms (women).
◊◊ Prolonged QTc if ≥470 ms (men) or ≥480 ms (women)

Results

- 1030 ECGs included (604 patients, 1.8 [95% CI, 1-4] ECGs per patient).
- LQTSnet achieved excellent discriminatory capacity for detecting LQTS:
  - AUC 0.929 [0.893-0.960] internal validation.
  - AUC 0.957 [0.899-0.995] external validation.
- Distinguishing between LQTS type 1 and type 2:
  - AUC 0.953 [0.864-1.000] internal validation.
  - AUC 0.913 [0.861-0.955] external validation.
- LQTSnet performed significantly better than expert-measured QTc intervals for detecting LQTS, including in patients with normal/borderline QTc.

Conclusions

- This cross-sectional study represents an early demonstration of deep learning to improve the detection of congenital LQTS in resting ECGs, including concealed LQTS.
- Prediction of the two most common genetic subtypes is also feasible.
- Further research can validate deep learning models over an unselected general population referred for suspected LQTS to maximize their clinical utility.

Online App and Open Source Model

ecgtools

GitHub

https://ecgtools.heartsinrhythm.ca/

https://github.com/river/lqts