Supplementary Materials

Artificial intelligence streamlines diagnosis and assessment of prognosis in Brugada syndrome: a systematic review and meta-analysis

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Supplementary S1. Search strategy in Ovid MEDLINE, Embase, Scopus, and The Web of Science from database inception to inception to Nov 6, 2023

1. exp Brugada syndrome/
2. exp electrocardiogram/
3. (ecg or ekg or electrocardiogra*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]
4. 2 or 3
5. exp artificial intelligence/ or exp deep learning/ or exp machine learning/ or (AI or "artificial intelligence" or "classification algorithm*" or "computer heuristic*" or "decision support system*" or "decision tree" or "deep learning" or "data science" or "feature detection" or "generative pre-trained transformer" or "language learning model*" or "large language model*" or "learning algorithm*" or "machine learning" or (Markov adj3 model*) or ((multifactor* or multicriteria) adj3 ("decision analysis" or "decision making")) or "natural language process*" or "nearest neighbor*" or "neural network*" or "outlier detection" or "pattern recognition" or "random forest" or "representation learning" or "support vector machine*" or "transfer learning" or "Bing chat" or ChatGPT* or "Chat GPT" or "Google* Bard" or "IBM Watson" or "Microsoft* Bing" or OpenAI or "Open AI" or PathAI or "Path AI").mp.
6. 1 and 4 and 5

Artificial intelligence search filter:

Campbell SM, Kung J. Filter to Retrieve Studies Related to Artificial Intelligence from the OVID EMBASE Database. Geoffrey & Robyn Sperber Health Sciences Library, University of Alberta. Rev July 13, 2023.

https://docs.google.com/document/d/1eWyO0jv9_6FYsxyC5LUYwFe9eH_3h83-tPNZ6wmos18/edit#heading=h.ldbxqb34y1kj

Supplementary Table 2. Validation, data selection, preparation process, and model threshold selection

Study	Validation method	Study type	Data selection and preparation process	Model threshold selection
Tse *et al.* (2020)	2-fold cross-validation, external validation	Prognostic	ECG features included HR, PR interval, QRS duration, and QTc	Threshold was selected based on ROC curve
Romero *et al.* (2016)	10-fold cross validation	Prognostic	Preprocessing steps of ECGs included automatic QRS detection, baseline drift attenuation by cubic spline interpolation, and Butterworth low pass filtering for the purpose of denoising. ECG features used to train the model included morphological QRS features and HRV markers. Feature selection used a hybrid approach consisting of a simple filter algorithm and a sequential floating feature selection method	Threshold was selected based on ROC curve
Randazzo *et al.* (2023)	5-fold cross validation	Prognostic	ECG features were chosen based on the risk stratification guidelines for BrS. These features were manually extracted from selected ECGs (e.g., PR interval, QRS duration in V1, QT interval in V5, *etc*.). These were fed into an MLP and a BDT algorithm	NR
Lee *et al.* (2021)	5-fold cross validation	Prognostic	BrS patients were stratified based on symptoms at presentation (asymptomatic, syncope, or VT/VF). Cox regression was used to determine significant predictors of shorter time to VT/VF on follow-up. A random	Threshold was selected based on optimal precision and recall

			survival forest (RSF) model was then trained on latent features extracted by NMF on risk predictors according to a sensitivity analysis. 26 features were included (e.g., prior VT/VF, syncope, age, QTc interval, QRS axis)	
Romero *et al.* (2022)	Repeated 10-fold cross-validation	Prognostic	Pre-processing steps followed a similar method to Romero 2016. ECG features included properties of the QRS complex, STT interval, and heart rate recovery	Threshold was selected based on ROC curve
Lee *et al.* (2022)	5-fold cross validation	Prognostic	Pre-developed risk scores for developing VT/VF were analyzed by ROC. The best performing algorithm (Sierira score) was modified by adding additional risk factors identified via Cox regression to develop a modified risk score. 7 machine learning algorithms were also developed based on ECG data	Not applicable. F1, sensitivity, specificity, NPV, PPV, and accuracy are not reported
Nakamura *et al.* (2023)	5-fold cross validation	Prognostic	12-lead ECG used to train CNN to diagnose on a per ECG basis (individual ECG) and a per-patient basis (all ECGs taken for a given patient)	Threshold was selected based on ROC curve
Micheli *et al.* (2023)	double cross-validation (5 external and 4 internal folds)	Diagnostic	ECG leads V1 and V2 were inputted into a CNN	NR

Melo *et al.* (2023)	7-fold cross validation	Diagnostic	12-lead digital ECG was reduced to single de-noised heartbeats and are then inputted into the DNN	Used Youden's J statistic to select a threshold of 0.5
Zanchi *et al.* (2023)	10-fold cross validation	Diagnostic	P-wave features were used to train the model	NR
Liu *et al.* (2022)	5-fold cross validation, external validation (independent cohort from Japan)	Diagnostic	Developed a source network to diagnose RBBB and then used a transfer learning strategy to train a DNN to classify the type 1 Brugada pattern based on 12-lead ECG	Threshold was selected based on ROC curve, without preference for sensitivity
Liao *et al.* (2022)	external validation	Diagnostic	12-lead ECG data split into 3 training and 2 testing cohorts were created, the validated on an external "deployment" cohort	Model sensitivity was predefined at 50%, 80%, and 90%. Other parameters were measured in relation to the preset sensitivity. The best performing model with respect to F1 score was achieved with the model set to 90% sensitivity

ECG: electrocardiogram; HR: heart rate; HRV: heart rate variability; BrS: Brugada syndrome; MLP: multi-layered perceptron; BDT: boosted decision tree; VT/VF: ventricular tachycardia/ventricular fibrillation; ROC: receiver operating characteristic; CNN: convoluted neural network; DNN : deep neural network; RBBB: right bundle branch block; NR: not reported.

Supplementary Table 3. PROBAST Risk-of-bias assessment for prognostic studies

	Domain 1: participants		**Domain 2: predictors**		**Domain 3: outcome**		**Domain 4: analysis**		**Overall judgement**	
Study	A. Risk of bias	B. Concerns regarding applicability	A. Risk of bias	B. Concerns regarding applicability	A. Risk of bias	B. Concerns regarding applicability	A. Risk of bias		A. Risk of bias	B. Concerns regarding applicability
Lee *et al.* (2021)	Low	Low	Low	Low	Unclear	Low	Low		Unclear	Low
Nakamura *et al.* (2023)	Low	Low	Low	Low	Low	Low	Low		Low	Low
Lee *et al.* (2021)	Low	Low	Low	Low	Low	Low	Low		Low	Low
Randazzo *et al.* (2023)	Low	High	Low	Low	Low	Low	Low		High	Low
Romero *et al.* (2016)	Low	Low	Low	Low	High	Low	Low		High	Low
Lee *et al.* (2022)	Low	Low	Low	Low	Low	Low	High		High	Low
Tse *et al.* (2020)	Low	Low	Low	Low	Low	Low	Low		Low	Low
Romero et al. (2022)	Low	Low	Low	Low	Unclear	Low	Low		Unclear	Low

Wolff RF, Moons KGM, Riley RD, et al.; PROBAST Group†. PROBAST: a tool to assess the risk of bias and applicability of prediction model studies. *Ann Intern Med* 2019;170:51-58. doi: 10.7326/M18-1376. PMID: 30596875.

Supplementary Table 4. QUADAS-2 risk-of-bias assessment for diagnostic studies

	Domain 1: patient selection		**Domain 2: index test(s)**		**Domain 3: reference standard**		**Domain 4: flow and timing**	
Study	A. Risk of Bias	B. Concerns regarding applicability	A. Risk of Bias	B. Concerns regarding applicability	A. Risk of Bias	B. Concerns regarding applicability	A. Risk of Bias	
Zanchi *et al.*, 2023	Low	Low	Low	Low	Low	Low	Low	
Liao *et al.*, 2022	Low	Low	Low	Low	Low	Low	Low	
Liu *et al.*, 2022	High	Low	Low	Low	Low	Low	Low	
Melo *et al.*, 2023	Unclear	Low	Low	Low	Low	Low	Low	
Micheli *et al.*, 2023	Unclear	Unclear	Low	Low	Unclear	Low	Low	

Whiting PF, Rutjes AW, Westwood ME, et al.; QUADAS-2 Group. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med* 2011;155:529-36. doi: 10.7326/0003-4819-155-8-201110180-00009. PMID: 220070.