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Review

Application of multi-feature-based machine learning models to predict neurological outcomes of cardiac arrest

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ABSTRACT

Cardiac arrest (CA) is a major disease burden worldwide and has a poor prognosis. Early prediction of CA outcomes helps optimize the therapeutic regimen and improve patients' neurological function. As the current guidelines recommend, many factors can be used to evaluate the neurological outcomes of CA patients. Machine learning (ML) has strong analytical abilities and fast computing speed; thus, it plays an irreplaceable role in prediction model development. An increasing number of researchers are using ML algorithms to incorporate demographics, arrest characteristics, clinical variables, biomarkers, physical examination findings, electroencephalograms, imaging, and other factors with predictive value to construct multi-feature prediction models for neurological outcomes of CA survivors. In this review, we explore the current application of ML models using multiple features to predict the neurological outcomes of CA patients. Although the outcome prediction model is still in development, it has strong potential to become a powerful tool in clinical practice.

Introduction

Cardiac arrest (CA) is a life-threatening condition with high mortality. Approximately 380,000 deaths from CA of any cause are reported annually in the United States [1]. The prognosis of CA is extremely poor, mainly due to post-cardiac arrest brain injury (PCABI) caused by the absence of cerebral blood flow (CBF) and the subsequent cerebral ischemia–reperfusion injury after the return of spontaneous circulation (ROSC).

Early prediction of the neurological outcomes of CA patients helps ensure timely intervention and improved prognosis. For instance, actively implementing targeted measures such as Percutaneous Coronary Intervention (PCI), Coronary Artery Bypass Grafting (CABG), and pulmonary thrombectomy can fundamentally correct the etiology of CA, or employing advanced life support measures like Extracorporeal Membrane Oxygenation (ECMO) [2,3]. It is also crucial to avoid making decisions regarding Withdrawal of Life-Sustaining Treatment (WLST) at inappropriate times. The timing of prediction is primarily within 72 h of Intensive Care Unit (ICU) admission [4]. The selection of this time point is based on the likelihood of patients' recovery of neurological function and the risk of prematurely WLST, aligning with guidelines recommendations [5]. The latest European Resuscitation Council (ERC) and the European Society of Intensive Care Medicine (ESICM) guidelines proposed the principle for prognostication, utilizing a multi-modal approach that includes clinical examination, biomarkers, electrophysiological assessments, and neuroimaging to predict the neurological outcomes of CA patients [5]. However, the implementation of this method is greatly limited by the availability of diagnostic equipment.

To further explore methods for assessing the neurological prognosis of CA patients, researchers have conducted extensive studies. Among these studies, the most commonly used neurological function assessment scale is the Cerebral Performance Category (CPC), where it is generally accepted that CPC of 1–2 correspond to good neurological outcomes, and CPC of 3–5 correspond to poor neurological outcomes [6]. Numerous clinical scores have emerged for assessing neurological outcomes of CA patients. Traditional scores such as the Sequential Organ Failure Assessment (SOFA) and Acute Physiology and Chronic Health Evaluation (APACHE) II scores are widely used for assessing the severity of illness and have proved to be valuable in predicting neurological outcomes of CA patients, but these scores only have moderate discriminative ability [7,8]. Some novel scores utilize linear regression methods, such as the Out-of-Hospital Cardiac Arrest (OHCA) and Cardiac Arrest Hospital Prognosis (CAHP) scores, which both use logistic regression to establish independent prognostic factors, developing

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scoring systems for predicting poor neurological outcomes of OHCA patients and have been validated in multicenter external cohorts [9–11]. However, both of these scores involve no-flow time, which introduces significant subjective factors in the statistics, thus affecting their accuracy. The Good Outcome Following Attempted Resuscitation (GO-FAR) score stratifies the neurological outcomes of in-hospital cardiac arrest (IHCA) patients, but it contains mostly baseline disease states and does not contain dynamic physiological and biochemical indicators [12]. In recent years, machine learning (ML) has gained a lot of attention in various fields. ML is a science of artificial intelligence (AI), which is increasingly used in medicine and has substantial advantages in analyzing vast quantities of medical data [13]. ML relies on vast amounts of data to train models to learn and recognize disease patterns and trends. As the amount of data increases and computing power improves, ML models can be optimized and expanded to adapt to new problems and challenges. Clinical tools based on ML for early warning [14,15], subphenotype clustering [16,17], decision-making [18], and prognosis assessment [19,20] in CA patients are rapidly developing.

ML contribute to providing objective information regarding the neurological outcomes of CA patients and hold promising prospects for application. Numerous researchers have employed diverse algorithms to construct ML predictive models based on various features. Therefore, in this review, we reviewed relevant ML studies of CA and focused on valuable predictive features for the neurological outcomes of CA patients, elaborating on the characteristics of these features and their current application in ML models. We tried to reveal how current ML studies excavate and integrate feature information to optimize feature engineering and enhance predictive performance. The novelty of this article lies in the fact that, firstly, we mainly focused on neurological prognosis of CA by using ML methods, which differ from reviews about conventional prognostic assessment methods and have a more precise scope. Secondly, we concentrated on the current state of researches in ML methods for integrating and excavating valuable predictive features, such as the construction of multi-modal ML models, and innovative predictive approaches based on ML image processing, with more detailed descriptions. Our aim is to assist clinicians in expanding new ideas for prognosis assessment, understanding valuable prognostic indicators and innovative feature processing methods, and promoting the greater role of ML in clinical practice.

Box 1 summary of search strategy and paper selection.

We searched MEDLINE from inception to June 2024 using terms to interpret cardiac arrest (cardiac arrest, heart arrest, arrest, out-of-hospital cardiac arrest, in-hospital cardiac arrest, cardiopulmonary resuscitation, resuscitation), terms of machine learning (machine learning, deep learning, supervised learning, unsupervised learning, reinforcement learning, logistic regression, random forest, decision trees, naive bayes, k-nearest neighbor, support vector machines, neural network, boosting, bagging), and terms for neurological outcomes (neurological outcomes, neurological prognosis, neuroprognostication, outcome, prognosis, neurological function, neurological recovery). We included only papers published in English.

Machine learning in CA

As clinical data volume expands and computing power increases, ML is becoming increasingly important in medicine [21]. ML can automatically complete tasks using computer-based data through various algorithms. Table 1 shows some key algorithms. ML can fall into supervised, unsupervised, and reinforcement learning; each category is applicable to different specific tasks, as shown in Fig. 1.

Supervised learning requires labeled data for model training, and aims to label the unidentified data by mapping input and output variables [21]. Supervised learning focuses on building predictive models. Supervised learning plays an important role in early warning of IHCA; such early identification of high-risk patients can alert clinicians to take action in advance. Li et al. screened seven critical variables and developed a prediction model to assess the risk of IHCA in patients hospitalized for acute coronary syndrome (ACS); this model demonstrated an area under the receiver operating characteristic curve (AUC) of 0.844 based on DT [22]. In another study on ACS, researchers developed eight models using multivariate clinical features to predict IHCA 24 h before its occurrence. Most of these models performed better than commonly used risk scoring, such as the National Early Warning Score (NEWS) and Modified Early Warning Score (MEWS), with XGBoost achieving the best performance (AUC: 0.958) [15]. For sepsis, a stacking ensemble model has been developed that can alert for IHCA within 6 h before CA occurrence with an accuracy and sensitivity exceeding 70 %. Supervised learning is also widely employed in CA prognostic models, which are described in detail in the next section.

Table 1
Definition of common ML algorithm terms.

Terms	Definition
Logistic Regression (LR)	A generalized linear regression analysis model based on a particular function outputs a value between 0 and 1, which is better suited to solving binary problems than simple linear regression.
Naive Bayes (NB)	A classification algorithm based on Bayesian decision theory, naive means to assume individual features are independent of each other.
k-Nearest Neighbor (kNN)	A model directly use training sets for classification or regression, finding k numbers of labeled datapoints closest to the new input.
Support Vector Machines (SVM)	A supervised learning binary classifier depending on decision boundary which maximises the distance from hyperplane to learning samples in feature space.
Random Forest (RF)	A type of decision trees that is essentially the collection of a large number of classification trees or regression trees, with higher accuracy and generalization ability.
eXtreme Gradient Boosting (XGBoost)	An end-to-end boosting tree system, which is the optimized gradient boosting decision tree (GBDT), capable of faster and more efficient training models.
Artificial Neural Networks (ANN)	A complex network of a vast number of processing units (neurons) with connected layers of nodes, which is a simplification and simulation of the human brain, having great advantages in processing complex data.
Convolutional Neural Networks (CNN)	A deep learning algorithm based on feedforward neural networks with convolutional computation, which can directly extract high-level features from structured data.

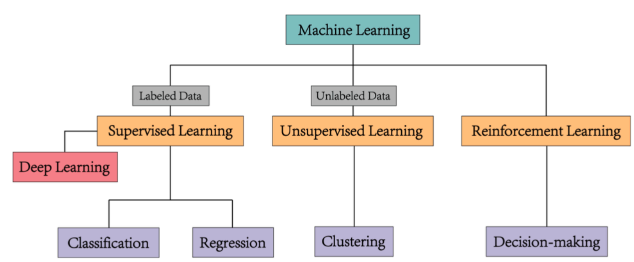

Fig. 1. Categories and tasks of ML.

Unsupervised learning uses unlabeled data to discover underlying clusters or groups in the feature space [21]. Different subphenotypes are associated with specific risk factors, clinical symptoms, and responses to treatment, which contribute to further precise therapy. Okada et al. performed a cluster analysis of OHCA with shockable rhythm and non-shockable rhythm using latent class analysis [16,17]. Subphenotype differentiation enables new hypotheses regarding the pathogenesis and manifestations of CA, which is valuable for developing heterogeneous interventions. Different outcomes across subphenotypes have also been observed following extracorporeal cardiopulmonary resuscitation (ECPR), suggesting that the indications for ECPR should be carefully considered [17]. For further precise treatment, Elmer et al. developed an unsupervised learning model to identify five subphenotypes of brain injury after CA based on the multimodal features of neurological examinations, brain CT and EEG [23]. Researchers have explored the associations between outcomes and target temperature management (TTM), hemodynamic strategies, and cardiac interventions among different subphenotypes, demonstrating that cluster analysis can reveal the mechanisms underlying acute brain hypoxia injury, in turn increasing treatment efficacy.

In reinforcement learning, the computer agent operates in an interactive environment, performing specific actions and obtaining rewards or penalties as learning feedback [21]. Agents learn by repeated trials to maximize rewards and can then be applied in clinical decision making, for example, determining the adjustment of mechanical ventilation parameters or the dose of fluid therapy [24,25].

Deep learning (DL) is a promising subfield of ML that uses algorithms that mainly rely on neural networks [26,27]. DL is more technically demanding than traditional ML and can manage more complex tasks. For example, one study used Embedded Full Convolutional Networks (EFCN) to model decision-making and survival outcomes in OHCA patients to support the decision to perform coronary angiography on survivors [18]. Korean researchers published an early warning score (DEWS) trained on a recurrent neural network (RNN). This score showed high sensitivity in predicting IHCA and performed better than MEWS and other warning models [14,28]. Notably, DL has shown strong potential in helping identify, classify, and quantify medical images and physiological signals for better analysis and interpretation. Conventional ML algorithms process image data following artificially set features, while DL mainly benefits from its ability to extract task-related features autonomously and diversely [26]. Substantial advancements in computer vision stimulate its application in medical image analysis, such as image segmentation [29], image annotation [30] and diagnosis [31,32]. We discuss the application of DL in brain imaging and EEG to excavate features related to the neurological function of CA patients in the next section.

Multi-feature models for neuro-prognostication

ML-based prediction of neurological outcomes in CA survivors is attracting considerable interest among medical researchers. Multiple features have been incorporated into ML models based on the different algorithms (Fig. 2), which are described in detail below.

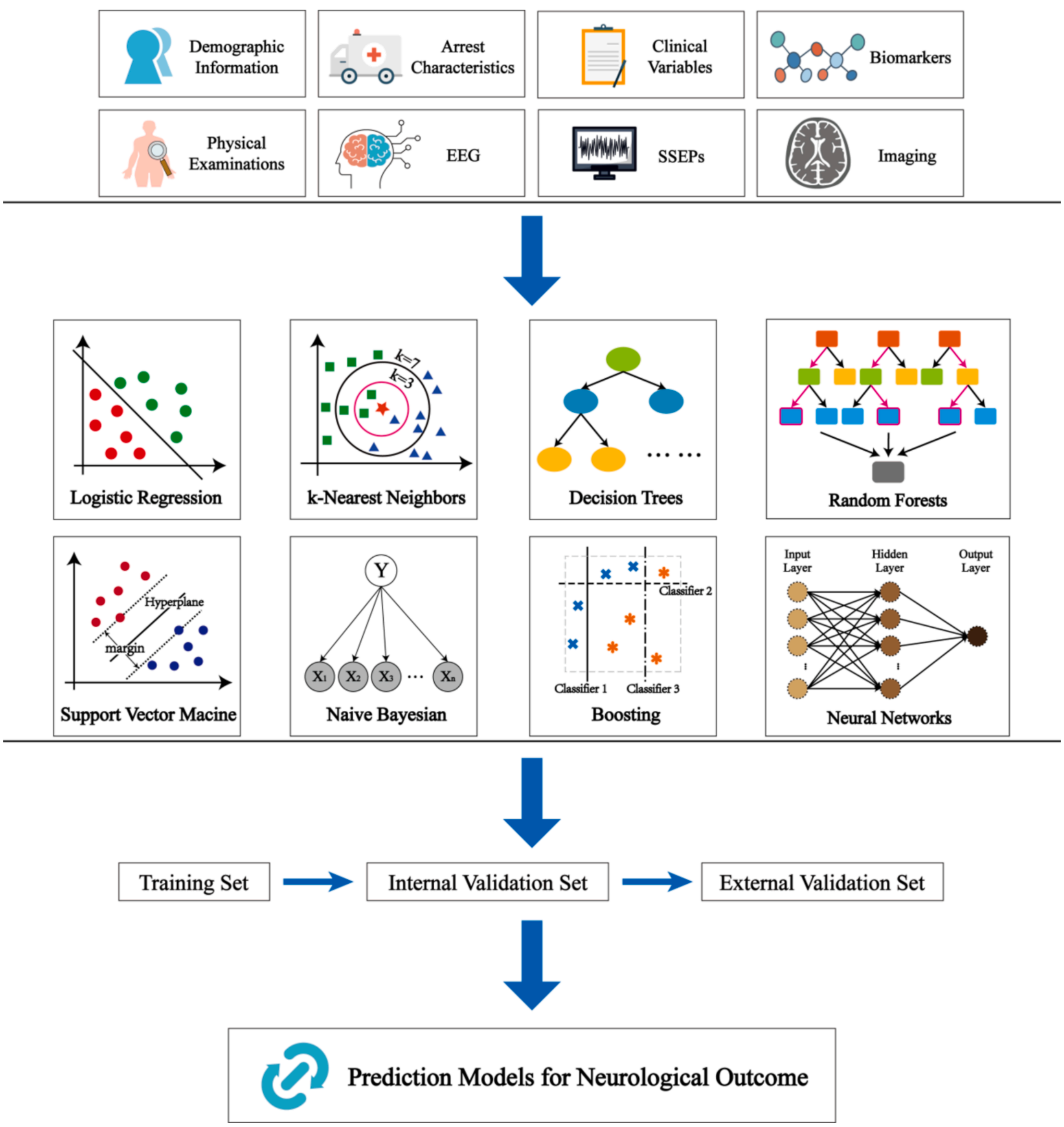

Fig. 2. Flowchart of prediction models for CA neurological outcomes.

Demography

Researchers generally include demographic information as the baseline characteristics for modeling, such as age, sex, and race. Some researchers have included body mass index (BMI) and demonstrated a U-shaped relationship between BMI and survival [33,34]. Recently, a model conducted using EFCN was reported, which creatively developed on community variables, including economic factors, basic health status, and crime conditions, to assess the neurological outcomes of OHCA patients at discharge [35]. Compared with clinical data alone, the final integrated model increased the AUC from 84.5 % to 88.1 %. Demography as the most basic feature contains a little prognostic information and is generally used as a cofactor to marginally increase model performance.

Arrest characteristics

CA-associated characteristics, such as the presumed etiology of arrest, initial heart rhythm, arrest location, and duration of resuscitation, are usually valuable for early outcome prediction. In addition, prehospital factors specific to OHCA are worth studying, such as witnessed status, bystander CPR, defibrillation, the presence of ROSC, and the EMS response time [36,37].

The Survival After ROSC in Cardiac Arrest (SARICA) scoring system was developed based on RF for predicting survival rate of OHCA patients at discharge [38]. This simplest model built on prehospital ROSC, age, and initial heart rhythm as the three most relevant features reached an AUC of 0.87. Two other RF-based models explored the relative importance of features; one listed initial rhythm and age as the top two predictors of outcome and the other prehospital ROSC and age [37,39]. In addition, bystander CPR may not increase predictive performance because of the overall quick EMS response in developed countries [38]. On the other hand, two researcher groups using XGBoost to predict neurological outcomes of OHCA patients at discharge achieved excellent capabilities and showed superior performance in comparison with other algorithms in discrimination and calibration [40,41]. They highlighted the importance of critical temporal variables, such as no flow time (from arrest until the start of CPR) and low flow time (from the start of CPR until the end of resuscitation) [42]. Others argued that these data may show large inaccuracies due to memory biases, and their model based on multi-layer perceptron (MLP) to predict neurological recovery (CPC 1 or 2) and survival to discharge reached an AUC of 0.953 without relevant time variables [43].

Regarding IHCA, two studies proposed by Mayampurath et al. showed XGBoost to be the optimal algorithm, significantly superior to traditional statistical methods and other ML models in predicting good neurological function at discharge [44,45]. This finding might be the fact that the large number of categorical variables make the inputs highly structured, and XGBoost is more flexible in considering non-linear relationships and interactions between features [46]. There are relatively few characteristics available for IHCA, and initial rhythm remains the most crucial predictor [44,45]. Consequently, arrest characteristics, including prehospital factors, are essential for the development of predictive models for the early assessment of CA patients' neurological function after admission. However, the accuracy of the relevant data may hinder its further application in the model.

Clinical variables

Clinical variables are mainly structured data containing substantial prognostic information in electronic health records (EHRs), including vital signs, laboratory results, medications, operations, and comorbid condition. Although excluded in current guidelines [5], clinical data are routinely selected by ML algorithms since these data are accessible and of high-capacity. One study screened key features from clinical variables alone with XGBoost achieving the best predictive power to assess favorable neurological outcomes at hospital discharge (AUC 0.956) [47]. Another study also demonstrated XGBoost to be the optimal model for predicting survival and neurological function of OHCA patients at discharge (AUC 0.87), indicating that physiological signals represent valuable prognostic information; in particular, features presenting in the first 24 h after arrest were associated with early recovery trajectories [48]. Our as-yet-unpublished model study identified 11 key features and visualized their significance using recursive feature elimination (RFE) and SHapley Additive exPlanations (SHAP). The CatBoost model we finally obtained reached an AUC of 0.86 for predicting neurological outcomes at discharge, which is especially suitable for the processing of categorical variables. Concluding the above three sections, relatively simple models for predicting the neurological outcomes of CA patients mainly include demographic information, arrest characteristics and clinical variables. In particular, improved ML algorithms, such as XGBoost, show better performance when processing low-dimension data.

Biomarkers

Biomarkers have been widely studied due to the easy accessibility and detection of samples. NSE, the product of neuronal insult, is the only biomarker recommended for prognostic assessment [5]. Although an NSE concentration exceeding 60 μg/L at 48–72 h after resuscitation is currently recommended as the valid predictor of poor outcome, its threshold with a 0 % False Positive Rate (FPR) remains controversial regarding the influence of mixed factors, such as extracerebral sources and measurement techniques [49,50]. S100 calcium-binding protein β (S-100β), the marker of astrocyte injury in prognostic assessment, is similarly controversial [49,50]. More large multicenter prospective validation studies are required to assess the threshold. In model development, researchers focused on whether biomarkers can improve the neurological prognostic ability of multi-feature models, for example, NSE can increased the AUC from 0.88 to 0.96 when involved in predicting unfavorable neurological outcomes at 3 months, with specificity up to 100 %[51].

Several research-grade novel biomarkers are promising for neurological outcome assessment, including neurofilament light chain (NFL) [52], glial fibrillary acidic protein (GFAP) [53], tau protein [54], and ubiquitin carboxyl hydrolase L1 (UCHL1) [55]. However, these markers appeared to be of marginal value when combined with conventional markers [56]. How to use valuable biomarker information for combinatorial modeling to maximize predictive performance and improve sensitivity should be investigated in the future.

Physical examination

Since neurological examinations directly reflect alterations in cerebral function, indicators such as brainstem reflexes, motor response, and myoclonus contribute to the prognosis assessment for CA survivors [49]. Persistent absence of the bilateral pupillary light reflex (PLR) is the best indicator, with satisfactory specificity (FPR 0–1 %) [57,58]. The predictive value of the absence of the corneal reflex (CR) is relatively weak and can be affected by neuromuscular blockers [59,60]. Abnormal flexion or a heightened response to pain (Glasgow Motor Score (GCS-M) $\leq$ 3) should be considered for adverse outcomes [61]. These examinations at 72 h or later after resuscitation have greater prognostic value; however, negative signs do not necessarily indicate favorable neurological outcomes [62]. Myoclonus with some features is associated with a poor outcome, such as that persisting for over 30 min (status myoclonus), early occurrence (<48 h), and often with malignant or unreactive EEG [63,64]. One study combined *peri*-arrest variables with GCS scores and PLR, establishing a model based on Fast-and-frugal decision trees to predict good neurological outcomes at 28 days [65], improving the sensitivity to 95–100 %. As indicated in the current guidelines, physical examinations play important roles in predictive algorithm;

however, more ML studies are multimodal since the combination of physical examinations and other features can often improve the consequence of prognostic assessment.

Electroencephalogram (EEG)

CA survivors are often comatose due to hypoxic ischemic encephalopathy (HIE). Continuous EEG monitoring allows the capture of substantial valid information that reflects the neurological function prognosis [50,66]. Previous studies have demonstrated that some EEG patterns are associated with neurological function changes, such as generalized EEG background suppression (amplitude < 10 μV), especially that persisting 24 h after arrest, which is indicative of poor outcomes [67–69]. Other malignant patterns, including burst suppression with identical bursts and some epileptiform activities, are valid indicators of severe cerebral ischemic injury [67–69]. Conversely, continuous and normal-amplitude EEG background patterns in recovery within 12 h after CA [68] and preserved EEG reactivity often correspond to favorable outcomes [70].

Despite the above, the high volume of EEG data and the subjectivity and variability of manual visual interpretation remain substantial challenges to the utilization of EEG information [71]. To solve this problem, Tjepkema et al. first introduced a concept combining five qEEG features called Cerebral Recovery Index (CRI) to assess neurological outcomes within 6 months. This index was validated to achieve a maximum AUC of 0.94 at 18 h after CA. Researchers have also demonstrated that the magnitude of CRI corresponds to adverse or favorable neurological outcomes in postanoxic patients within 24 h after CA. However, this index was developed from a handcrafted parametric model. Therefore, this research group optimized it in a subsequent study, and the number of qEEG features was increased to 9 with RF classifiers [72]. Unlike previous approaches that equally weighted all features, RF presented features with variable weights and, therefore, achieved the optimal feature combination. The improved index reached an AUC of 0.92 at 12 h. In Tjepkema's latest study for predicting 6-month neurological outcomes of CA patients, the revised Cerebral Recovery Index (rCRI) was introduced, which is based on 44 qEEG features [73]. The AUC of this advanced index developed from RF reached 0.94 at 12 h.

DL is equipped with an automated "feature extraction" pipeline, without depending on explicit input feature definition [26]. Therefore, DL is especially skilled at processing raw biological signals, which can make the utmost of the integral EEG spectrum, and even explore new features that cannot be identified by human reviewers. Convolutional neural network (CNN) shows the best performance and can also minimize the influence of artifacts and noise [74]. The association between some EEG patterns and the neurological outcomes is time-dependent; thus, the significance of EEG dynamics has recently been explored to improve the prognostic value outside of confinement to a definite time window [68,75]. Zheng et al. developed a multiscale CNN-LSTM model based on the temporal evolution of EEG [76]. The internal framework consisted of a CNN model that automatically extracts EEG features and a bidirectional long short-term memory (Bi-LSTM) model, a type of recurrent neural network, that incorporates the evolution of longitudinal EEG waveforms from multiple time scales in both forward and backward directions. Among all models developed from the same dataset, the proposed time-sensitive CNN-LSTM model showed the best performance in predicting neurological outcomes at 3–6 months after CA, which improved with EEG duration from an AUC of 0.83 at 12 h to an AUC of 0.91 at 66 h. Various studies have indicated that deep neural networks could analyze longitudinal EEG time trends to improve the model performance and possibly realize real-time neurological outcomes prediction for comatose patients after CA [76–78].

Electrophysiology

Short-latency somatosensory evoked potentials (SSEPs) are elicited by repetitive electrical stimulation of the median nerve, and the potentials are recorded from the cerebral sensory cortex. The negative waves of ~ 20 ms are referred to as N20 and reflect the activation of the primitive sensory cortex [79]. A bilateral absence of N20 or decreased amplitudes in comatose patients often indicates severe hypoxic ischemic brain injury [50,80,81], with 100 % specificity in predicting 6-month neurological outcomes at 12 h post-CA [82]. However, compared with EEG, the sensitivity of SSEPs is relatively low (only 20–40 %), and it only makes sense to use it to evaluate poor outcomes [83,84]. SSEPs are rarely included as the input features of prediction models alone. Some researchers discovered that the combined feature set showed better predictive performance than using EEG alone or clinical features (including corneal and pupil reflex, SSEPs, and imaging manifestations of hypoxia) [85]. Thus, the complementary predictive value of the combination of various features has been demonstrated.

Imaging

Brain imaging can help identify cerebral edema caused by anoxic-ischemic insult. For example, brain CT shows obvious structural alternations of reduced sulci and ventricle size [86]. Neuronal edema results in reduced gray matter density, further complicating the discrimination between gray and white matter as the interface becomes obscured. Thus, gray–white matter density ratio (GWR) can be used to define the degree of cerebral swelling [86]. A decreased GWR indicates a poor neurological outcome after resuscitation, with threshold variability due to different sampling areas and testing devices, achieving satisfactory specificity (93–99 %) and moderate sensitivity (29–60 %) overall [87]. This association is time-dependent, and the prognostic value of GWR at 12 h after ROSC may be limited. Two groups have developed algorithms to automatically decompose images and calculate GWR [88,89], which can eliminate the artificial error caused by manually placing regions of interest (ROIs). It was verified that such automated GWR determination accurately conducted the prediction of poor outcomes after CA.

Compared with CT scanning, brain MRI has a higher resolution and relatively higher sensitivity (69–87 %) [86]. In the acute stage after resuscitation, restricted diffusion caused by cytotoxic edema appears on the diffusion-weighted imaging (DWI) sequence as hyperintensity in the corresponding damaged areas, while apparent diffusion coefficient (ADC) values of the quantitative index show low attenuation [50,86]. In addition, fluid-attenuated inversion-recovery (FLAIR), T1-weighted (T1WI), and T2-weighted (T2WI) sequences display high signal areas as the disease progresses [86].

ML algorithms are generally applied in more advanced image processing and analysis. For example, cortical thickness and subcortical gray matter volume have been measured to accurately assess the effect of anoxic–ischemic injury on long-term outcomes after CA. The multivariate supervised learning model based on morphological data suggested that atrophy of the hippocampus and other anatomic sites was associated with remaining disability and death, with an AUC of 0.96 for predicting neurological outcomes at 1 year after CA [90]. Several other studies have been conducted on resting-state functional MRI (rs-fMRI), which has been applied successfully to assess the state of consciousness in patients with brain injury [91,92]. Researchers compared the predictability based on rs-fMRI with that based on DWI, and the former achieved significantly better performance at predicting coma outcomes during hospitalization in CA patients (AUC of 0.94 vs. 0.63) [93]. DL can extract features independently from information; thus, it is widely used in image analysis [94]. One recent study designed a CNN framework to automatically capture and analyze raw structural and functional MRI data, and the findings suggested that fMRI data was more effective for identifying patients 3-month neurological outcomes than sMRI (accuracy 96 % vs. 82 %) [95]. In addition, the influence of each index on the output is visually interpreted by a voxel-based visualization tool developed from CNN filters, avoiding the potential black box effect of CNN [95].

Limitations and prospections

ML is increasingly integrated with multi-feature predictors in predictive models for neurological outcomes of CA survivors; however, some limitations remain. Firstly, as a classifier model, AUC is the primary performance metric, and both specificity and sensitivity are crucial. High specificity helps avoid misdiagnoses and unnecessary treatments, while high sensitivity helps prevent missed diagnoses. ML can integrate features and continuously optimize parameters, but often falls short in balancing sensitivity and specificity. For instance, So et al. constructed a tree model that included features such as age, gender, initial rhythm, no-flow time, low-flow time, pupillary light reflex, and GCS score, achieving 100 % sensitivity but only 64 % specificity [65]. Peluso et al. reported a multimodal approach that integrated neurological pupillary index, NSE, EEG, and SSEP, with specificity and sensitivity of 100 % and 70 %, respectively [51]. Therefore, further studies are required to optimize feature organization to better balance sensitivity and specificity. Additionally, calibration is also a very important concept, which indicating the consistency between the predicted probabilities and the actual occurrence; only well-calibrated models can exhibit strong robustness in clinical settings. Second, different ML algorithms have their own strengths, but there is still no optimum model. The potential difficulty in selection lies in the differences in the intrinsic data characteristics and research design, complicating comparisons across models. In addition, there are bound to be differences in the integrity of neurological function of CA patients at different study endpoints, and we still cannot determine a single algorithm. Researchers have attempted to construct predictive models based on ensemble algorithms, which may be a promising direction for designing more robust and practical models in the future. Third, most ML models extracted training samples from regional datasets and were limited to single-center internal validation. Some studies used two independent open-access databases to train and externally validate neurological prognostic models [48,96]. Few studies used unique cohorts for external validation on the basis of previous studies [97]. Therefore, more multicenter, prospective studies are needed to validate model generalizability. Besides, multicenter validation may not produce desirable results due to inherent different patient spectrum. Considering the above limitations, no single ML model for predicting neurological outcomes after CA has been widely applied in clinical practice.

With the increasing volume of medical data and the gradual maturity of ML technology, the effective combination of medicine and informatics is an inevitable trend. ML, with its high speed and precision, saves a lot of labor costs and time waste and helps clinicians obtain more accurate neurological outcome assessments in the early stages, make WLST decisions, and optimize the allocation of medical resources. ML approaches can also guide clinical treatment and improve patients' quality of life after discharge. In addition, although the latest guidelines recommend multimodal prognostic assessment with clinical neurological examinations as the main components, these guidelines exclude demographics, prehospital information, and arrest characteristics [5]. ML can integrate various features to improve the overall performance of the prediction models. The guidelines indicate that manifestations of anoxic injury on CT or MRI are associated with poor outcomes. However, current imaging research based on DL focused on neural network connectivity has generated novel directions for image-related prognostic analysis. Moreover, an increasing number of ML-related clinical studies have been conducted, and researchers worldwide have engaged in independent model development and validation. These researchers are striving to widely apply ML-based neurological outcome prediction tools. Further research on predictors, such as more advanced biomarkers, EEG, and rs-fMRI, will likely enhance their clinical accessibility, leading these approaches to become common clinical detection methods in the future.

Conclusion

Early assessment of the outcomes of CA survivors contributes to clinical decision-making and further intervention. Numerous features have been found to be valuable in predicting the neurological outcomes of CA patients, such as arrest characteristics, biomarkers, SSEPs, and EEG. ML has unique advantages in processing and analyzing high-capacity data and constructing predictive models. In particular, much research has been conducted on supervised learning and DL algorithms. Although ML models have not been widely applied in clinical practice, this approach has broad prospects for future explorations and will likely become a powerful tool to evaluate CA survivor outcomes.

Author contributions

PN planned the manuscript. PN and SZ conducted the literature search and drafted the manuscript. MD and WH revised the manuscript. All authors contributed to manuscript revision and approved the submitted version.

CRediT authorship contribution statement

Peifeng Ni: Writing – original draft, Methodology, Investigation, Conceptualization. **Sheng Zhang:** Writing – review & editing, Methodology, Conceptualization. **Wei Hu:** Writing – review & editing, Supervision, Funding acquisition. **Mengyuan Diao:** Writing – review & editing, Supervision, Methodology, Conceptualization.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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