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Effect of Esketamine on perioperative anxiety and depression in women with systemic tumors based on big data medical background

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Abstract. – OBJECTIVE: Perioperative anxiety and depression syndrome (PADS) is a common clinical concern among women with systemic tumors. Esketamine has been considered for its potential to alleviate anxiety and depressive symptoms. However, its specific application and effectiveness in PADS among women with systemic tumors remain unclear. This study aimed to analyze the utility of Machine Learning (ML) algorithms based on electroencephalogram (EEG) signals in evaluating perioperative anxiety and depression in women with systemic tumors treated with Esketamine, utilizing a large-scale medical data background.

PATIENTS AND METHODS: A single-center, randomized, placebo-controlled (SC-RPC) trial design was adopted. A total of 112 female patients with systemic tumors and PADS who received Esketamine treatment were included as study participants. A moderate dose (0.7 mg/kg) of Esketamine was administered through intravenous infusion over a duration of 60 minutes. EEG signals were collected from all patients, and the EEG signal features of individuals with depression were compared to those without depression. In this study, a Support Vector Machine (SVM)-K-Nearest Neighbour (KNN) hybrid classifier was constructed based on SVM and KNN algorithms. Using the EEG signals, the classifier was utilized to assess the anxiety and depression status of the patients. The predictive performance of the classifier was evaluated using accuracy, sensitivity, and specificity measures.

RESULTS: The C2 correntropy feature of the delta rhythm in the left-brain EEG signal was significantly higher in individuals with depression compared to those without depression (*p*<0.05). Moreover, the C2 correntropy feature of the Alpha, Beta, and Gamma rhythms in the left-brain EEG signal was significantly lower in individuals with depression compared to those without depression (*p*<0.05). In the right brain EEG signal, the C2 correntropy feature of the delta rhythm was significantly higher in individuals with depression (*p*<0.05), while the C2 correntropy feature of the alpha and gamma rhythms was significantly lower in individuals with depression compared to those without depression (*p*<0.05). Additionally, the C1 correntropy feature of the Gamma rhythm in the right brain EEG signal was significantly higher in individuals with depression compared to those without depression (*p*<0.05). The SVM classifier achieved accuracy, sensitivity, and specificity of 98.23%, 98.10%, and 98.56%, respectively, in recognizing the left-brain EEG signals, with a correlation coefficient of 0.95. In recognizing the right brain EEG signals, the SVM classifier achieved accuracy, sensitivity, and specificity of 98.74%, 98.43%, and 99.03%, respectively, with a correlation coefficient of 0.96. The improved SVM-KNN approach yielded an accuracy, recall, precision, F-score, area over the curve (AOC), and Receiver Operation Characteristics (ROC) of 0.829, 0.811, 0.791, 0.853, 0.787, and 0.877, respectively, in predicting anxiety. For predicting depression, the accuracy, recall, precision, F-score, AOC, and ROC were 0.869, 0.842, 0.831, 0.893, 0.827, and 0.917, respectively.

CONCLUSIONS: Significant differences were observed in the brain EEG signals between individuals with depression and those without depression. The improved SVM-KNN algorithm developed in this study demonstrates good predictive capability for anxiety and depression.

Key Words:
Big Data Medicine, Esketamine, Patients with systemic tumors, Perioperative period, Anxious, Depressed.

Introduction

Perioperative anxiety and depression refer to anxiety and depressive symptoms associated with the preoperative, intraoperative, and postopera-

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tive periods. Anxiety and depression are common psychological issues during the perioperative period[1]. Perioperative anxiety is often characterized by fear of surgery, concerns about surgical outcomes, unease regarding preoperative examinations and preparations, as well as anxiety about postoperative recovery. Anxiety may lead to physiological responses such as increased heart rate, elevated blood pressure, and rapid breathing[2,3]. It can also increase anesthesia and surgical risks[4]. Furthermore, anxiety can interfere with postoperative recovery and rehabilitation, prolong hospital stay, and increase medical expenses[5]. Depression, on the other hand, is a persistent emotional state characterized by sadness, grief, and loss of interest. Perioperative depression is commonly manifested as low mood, lack of motivation, loss of interest and pleasure, as well as a negative attitude towards the recovery process[6]. Depression may cause physiological and psychological changes such as decreased appetite, weight loss, and sleep disturbances[7]. It can also lead to reduced treatment compliance, increased risk of postoperative complications, and even impact the quality of life and social functioning[8]. These psychological issues not only affect the mental well-being of patients but may also have a negative impact on surgical outcomes, the recovery process, and overall quality of life. Sadness is indeed a common aspect of human existence in response to unfavorable circumstances and events. It is considered a normal emotional state if it is temporary and transient. However, if sadness persists for an extended duration, seeking medical advice becomes crucial for appropriate intervention. Table I presents the prevalence of depressive disorders within the population and annual suicide rates attributed to depression[9].

Esketamine, as an atypical antidepressant, exhibits rapid antidepressant effects[10]. Its antidepressant action is related to its modulation of glutamate receptors in the central nervous system, promoting synaptic plasticity between neurons and restoring neurotransmitter balance. This mechanism facilitates normal communication between neurons in patients with depression, leading to an improvement in neurotransmitter balance and a reduction in depressive and anxiety symptoms[11]. In addition to its antidepressant effects, Esketamine possesses various properties, including analgesic, anti-inflammatory, and antioxidant effects[12,13], which may have positive impacts on patients during the perioperative period. Studies[14] have found that Esketamine can counteract treatment resistance and demonstrate efficacy in patients with both unipolar and treatment-resistant depression. Esketamine has been investigated for its potential to alleviate perioperative pain and reduce the need for sedative agents[15]. It has been shown to reduce postoperative pain and prolong analgesic effects, promoting faster recovery in patients[16]. However, the specific application and effectiveness of Esketamine in perioperative anxiety and depression among women with systemic tumors remain unclear.

Machine Learning (ML) is a significant field within artificial intelligence that focuses on the development and optimization of algorithms and models. Its primary objective is to enable automated prediction and decision-making processes. ML has enormous benefits for the medical profession. Regression and classification models are established using ML algorithms to aid in the diagnosis of various diseases and drug administration[17]. Most of the methods that other researchers earlier used in finding out the depression disorders in patients were mainly based on ML algorithms[18-20]. Comparative studies related to the various types of depression have been analyzed by means of deep learning techniques by Rosner et al[21]. Liu et al[22] list have put forth a method that automatically detects depression with the help of convolutional neural networks. Tamman et al[23] have proposed a technique through which anxiety and depression can be detected with electronic health data. Bahji et al[24] have carried out another similar work. They have demonstrated a computer-based electronic depression system. Several researches[25,26] have

Table I. Portion of the population suffering from depression[9].

Parameter	Number of affected people	Portion affected in percentage
Total population affected	280	3.8%
Adults less than 60 years	14	5.0%
Adults above 60 years	16.24	5.8%
Suicide case each year	0.7	0.25%

also investigated the identification of depression disorders in patients using facial expressions and eye movements. Support Vector Machines (SVM) is a supervised ML algorithm that enables decision-making and is employed to mitigate noisy data in order to achieve better outcomes[27]. This classifier is a statistical model used for classification and regression problems. The use of ML approaches to forecast stress and mental health conditions will have a huge impact. The human body suffers from these mental health conditions because they cause the immune system to be suppressed, which raises the risk of contracting numerous infectious diseases.

To investigate the impact of Esketamine on perioperative anxiety and depression in women with systemic tumors, a single-center, randomized, placebo-controlled (SC-RPC) trial design within the framework of a large-scale medical data background was employed. A total of 112 female patients with systemic tumor-associated perioperative anxiety and depression syndrome (PADS) were included as research subjects. The patients were administered a moderate dose of 0.7 mg/kg Esketamine through intravenous infusion over a duration of 60 minutes. With the aid of an improved SVM-K-Nearest Neighbour (KNN) hybrid classifier, the study aimed to assess the application effects of Esketamine in perioperative anxiety and depression among women with systemic tumors. This investigation sought to reveal the impact of Esketamine on the mental well-being of perioperative anxiety and depression patients and provide further insights into the potential of Esketamine as a treatment for perioperative anxiety and depression. The findings aim to offer reliable evidence and guidance for clinical practice.

Patients and Methods

The methods implemented in this research are based on a SC-RPC trial. The patients under the treatment are recruited after proper screening and analysis. The SC-RPC trial lasted for two years, from 2019 to 2021. The selected patients were all female individuals with systemic tumors. The patients involved in this research are analyzed and screened by two doctors and 4 nurses. All of the experimental procedures conducted in this study were approved by the Animal Ethics Committee of Shandong University of Traditional Chinese Medicine.

Clinical Data

Population of study

Patients with systemic tumors who have received postoperative treatment with Esketamine are screened and selected based on eligibility criteria. The inclusion criteria consider patients aged between 18 and 50 years, and they are divided into two categories. Patients with low to medium depressive symptoms are classified as DP_1, while patients with medium to high depressive symptoms are classified as DP_2. Both categories of patients are expected to remain hospitalized for approximately 10 days.

When selecting patients, anaesthesiologists may consider classifying them as IV or V and take into account any history of epilepsy. Additionally, patients who have received anti-depressant medication within three weeks may be evaluated for the presence of depressive disorder. The illness was due to psychiatry, allergic history, drug-related abuses, a history of body mass greater than 30 kg/m^2 and the heart rate greater than 120 beats per minute, the blood pressure during contraction is greater than 180 mmHg, and during relaxation is greater than 90-mmHg, and prehypertension is greater than 140 mmHg for systolic and greater than 90 mmHg for diastolic, failure in heart, Parkinson related syndrome, liver dysfunction and the tumor identified in the systemic areas and the patients who were not supporting the psychiatric assessments and pregnant women are included in this research. The inclusion of study participants and treatment protocols, along with other procedural information, is depicted in Figure 1.

Assessment methods for anxiety and depression

The anxiety and depression of the patients were evaluated *via* the Patient Health Questionnaire (PHQ-15, PHQ-9) and Montgomery-Åsberg Depression Rating Scale (MADRS), which is measured and predicted by well-trained psychiatric professionals on the day before the surgery. The PHQ-15 comprises 15 questions, including stomach pain, lower back pain, pain in other body parts (arms/legs), joint pain (knees/hips), headaches, chest pain, dizziness, fainting, rapid heartbeat, shortness of breath, constipation/digestive problems/loose bowels, nausea, stomach problems, fatigue, sleep problems, and menstrual pain. Each question is assessed using the categories "Not Considered," "Little Consideration," and "More Consideration," with a score of 0 assigned to "Not

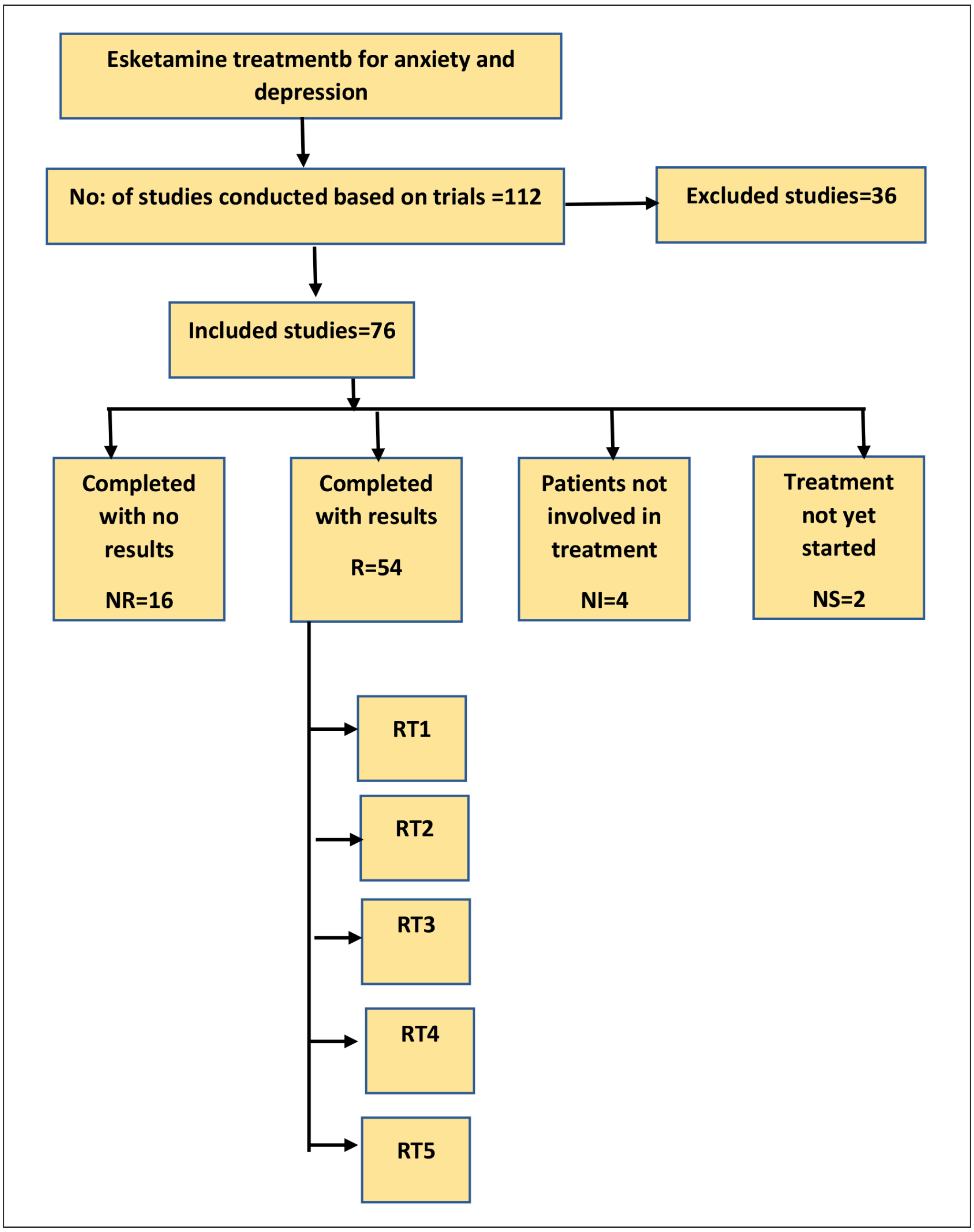

Figure 1. Flow chart for selection of SC-RPC on Esketamine.

Considered," a score of 1 assigned to "Little Consideration," and a score of 2 assigned to "More Consideration."

The PHQ-9 consists of 9 questions, including loss of interest in activities, depressive symptoms, increased sleep, feeling tired, overeating or poor appetite, feeling bad about oneself, difficulty concentrating, speaking slowly, and self-harm. Each question is evaluated using the categories "Not Considered," "Little Consideration," and "More Consideration," with a score of 0 assigned to "Not Considered," a score of 1 assigned to "Little Consideration," and a score of 2 assigned to "More Consideration."

The questionnaire used for predicting the patient's health condition may vary for different cases, as it is specific to the model used in our study. It is important to note that the ranges indicating the levels of low, medium, and severe issues for different questionnaires may differ. These ranges are described in Table II. The scoring for PHQ-15 is categorized as follows: 0-5, 6-10, 11-15, 16-20,

Table II. Prediction Range of PHQ-9, PHQ-15, and MADRS.

Range	Severity of depression	Range	Severity of depression	Range	Severity of depression
0-4	Very Low	0-5	Very Low	0-6	Very Low
5-9	Low	6-10	Low	7-12	Low
10-14	Medium	11-15	Medium	13-20	Medium
15-19	High	16-20	High	21-34	High
20-25	Very High	21-30	Very High	>34	Very High

and 21-30 points. For PHQ-9, the scoring ranges are: 0-4, 5-9, 10-14, 15-19, and 20-25 points. The score of MADRS ranges from (0-6, 7-12, 13-20, 21-34, >34) are needed for diagnosing the low level to high level depression symptoms.

From the overall analysis, the depression range is evaluated from the patient's health questionnaire PHQ-9, PHQ-15, and MADRS which is determined in such a way that the score range less than 14 shows moderate severity for PHQ-9 and less than 15 shows moderate severity for PHQ-15 and less than 20 shows moderate severity for MADRS. The assessment of moderate to severe PADS was conducted using PHQ-15, PHQ-9, and MADRS scales. The specific assessment procedures and methods are illustrated in Figure 2.

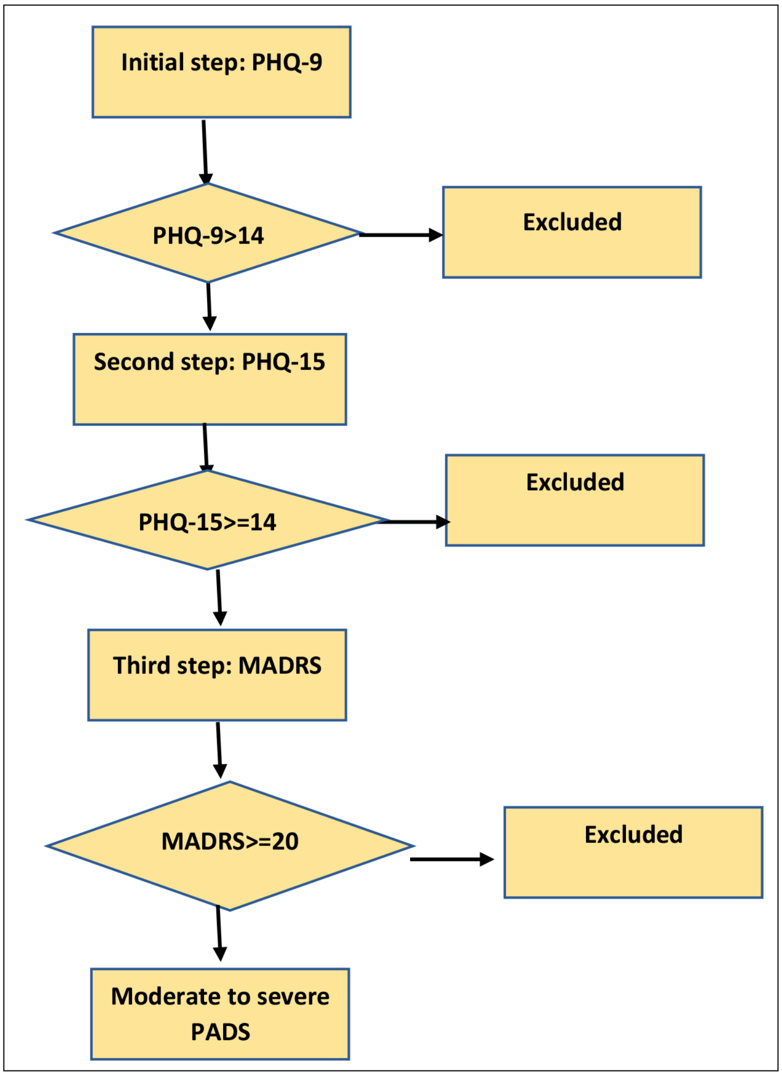

Figure 2. Flow chart of psychiatric assessment and diagnosis process (PHQ-9, PHQ-15, MADRS).

Table III. Portion of the population suffering from depression[9].

Medication	Dosage
Midazolam	0.05 mg/kg
Propofol	1-3 mg/kg
Etomidate	0.2-0.5 mg/ml
Sufentanil	0.2-0.4 μg/kg
Rocuronium	0.6 mg/kg
Cisatracurium	0.2 mg/kg

Grouping and Treatment Methods

The research assistant is prohibited from participating in anesthesia management, data collection, medication administration, and follow-up visits. The patients enrolled in this treatment were randomly divided into SC-RPC and Esketamine groups. In the Esketamine group, patients were administered a minimum dosage of 0.5 mg/kg to 0.7 mg/kg based on body weight, and the infusion was continued for at least 60 minutes. Similarly, in the SC-RPC group, the same dosage was administered at a comparable infusion rate. All solutions were injected at an approximate rate over a duration of 60 minutes. The solutions obtained after the investigation are managed and administered by the primary anesthesiologist, who is not involved in any other aspect of the treatment. The perioperative anesthesia management protocol includes monitoring ASA parameters such as ECG for heart activity, pulse oxygen saturation, non-invasive blood pressure, body temperature, and other relevant parameters. Peripheral venous access and peripheral artery catheterization are established prior to anesthesia induction. Health parameters, including arterial pressure, pulse rate, and urine output, are continuously monitored.

The process of randomization involves blinding the randomized blocks through a computer system stratifying the blocks based on the severity of PADS into very low, low, medium, high, and very high categories. Patients diagnosed with PADS are randomly assigned to receive Esketamine. The randomized trials are securely enveloped and managed by an independent person not involved in the analysis. The anesthesiologists, patients, and assessors are blinded to the treatment groups, ensuring their presence and active participation in the analysis while maintaining confidentiality.

The Esketamine and the SC-RPC are made into 30 mL-50 mL volumes, and from this, the Esketamine concentration is increased from 1 mg/ml to 3 mg/mL. The solution under investigation could be labeled as a "trial solution" and further researched according to a randomization sequence.

The additional medicines administrated to the patient after the Esketamine treatment are given in Table III.

Mechanical ventilation is carefully managed to deliver a tidal volume ranging from 6 mL/kg to 8 mL/kg, with a respiratory frequency of approximately 15 to 20 breaths per minute. The inhalation and exhalation ratio is set at 1:2, while the inhaled oxygen concentration is maintained at around 60% of the total flow rate. The flow of fresh gas is adjusted within the range of 1 L/min to 2 L/min to ensure the end-tidal carbon dioxide ($ETCO_2$) level remains between 30 and 46 cm H_2O. Medications such as remifentanil and propofol are administered within prescribed limits to control postoperative nausea and vomiting. In cases of severe PADS, additional measures are implemented, including informing the surgical ward doctors and nurses and providing professional consultation if necessary.

Medical Decision-Making Based on Big Data Medical Background

Electronic medical records are utilized in modern healthcare systems to facilitate the monitoring and storage of patient data, including comprehensive summaries of numerous clinical cases. The level of formalization of medical data within a Medical Information System (MIS) may vary. The MIS models the diagnosis and treatment processes by capturing and organizing relevant events that reflect the activities related to patient care. Clinical data describing the patient's condition is often available in a less formalized format, such as plain text. In this study, a discrete controlled process model is employed, introducing the concepts of control (C) and state (S). Controls primarily refer to diagnostic activities and treatment decisions that will be executed in the future. These controls encompass a wide range of treatments and diagnostic activities prescribed by healthcare professionals, including tests for disease diagnosis, administration of medications, and surgical interventions. The treatment approach is determined by the physician's medical expertise, and in this study, the focus is on diagnosing the impact of Esketamine on perioperative anxiety and depression in women with systemic tumors. The treatment and diagnostic processes are carefully controlled and guided by experienced healthcare professionals. The diagnostic scope encompasses previous measures that have been proven to enhance effectiveness. This research specifically targets the identification of anxiety and depression among female patients suffering from systemic tumors who have received Esketamine. Data from a total of 112 patients were collected through direct investigations and classified using a modified support vector machine. The patients included in this study fall within the age range of 20 to 50 years. Table IV shows questionnaires used for predicting anxiety and depression.

The participants' responses were encoded with numeric values ranging from 0 to 3, and the scores were calculated using formula (1).

(1)

Score = R*2

Where, R = sum of rating points of each class.

After calculating the final scores, the labeling was done based on the severities: very low, low, medium, high, very high (Table V).

Establishment of Anxiety and Depression Assessment Model Based on ML Method

The Big data platform is employed to classify the percentage of individuals experiencing anxiety and depression using ML techniques. The R programming language is utilized for predicting anxiety and depression levels based on severity. The dataset consists of real-world data analysis as well as clinical data retrieved from a cloud database. The entire dataset is divided into a training dataset (representing 50% of the data) and a testing dataset (representing 80% of the data). The methodology employed by the modified SVM-KNN classifier is described in detail in the subsequent section.

Modified hybrid SVM-KNN classifier

The support vector machine and K-nearest neighbor work for regression along with classification-oriented tasks mainly for classification. The classifying and presenting ability of these applications are divided into two different classes with certain distances, and the distance of separation is increased to make it suitable for any kind of function. The usage of KNN makes the system adapt to the recent valid points for information sharing. The modification made in this hybrid model has increased its efficiency in the classification of multiclass functions. The algorithm gets started with the process of initializing the k neighbors followed by the training features and test features.

In the proposed method, adaptive wavelet transform is applied to the electroencephalogram signals. By utilizing the rhythm analyzed from the electroencephalogram (EEG) signals, the centered correntropy is evaluated. The features are obtained by using the statistical test (Kruskal-Wallis). The output received through the statistical test is applied to the classifiers. Here, SVM and KNN classifiers are used. Popova et al[14] has utilized convolutional neural network-based EEG signal analysis for depression detection. The output of the classifier segregated the depressive and non-depressive sets. The flow diagram of the proposed method is illustrated in Figure 3.

The input signal (EEG)

EEG signals are used as the input signal[28-30]. The acquisition of data was achieved from the patients in their rest state in two categories. One was done with the eyes open and the other with the eyes closed. EEG signals were recorded from the right and the left halves of the brain with the use of bipolar assortment. The blinking and the movement of the patients' eyes were eliminated. The effects of the muscle movement were also discarded. The EEG signals that were sampled at 250 hertz and 50 hertz were removed using a notch filter. For easier analysis, the EEG signal was segmented into five hundred smaller parts at two-second interval.

Segregation of rhythm

The adaptive wavelet transform is used to extract the five rhythms of the electroencephalo-

Table IV. Questionnaires on anxiety and depression.

Anxiety	Depression
Mouth dryness	Negative feeling
Breathing problem	Initiation problem
Shivering problem	Lack of concentration
Getting panic	Fed up with the downhearted
Worried about panic	Enthusiastic problem
Heart throbbing	Not considering himself as a person
Getting scared	Feeling life was meaningless

Table V. Various severity levels.

Level of severity	Anxiety	Depression
Very low	0-5	0-7
Low	6-10	8-10
Medium	11-15	11-14
High	16-20	15-22
Very high	>20	>22

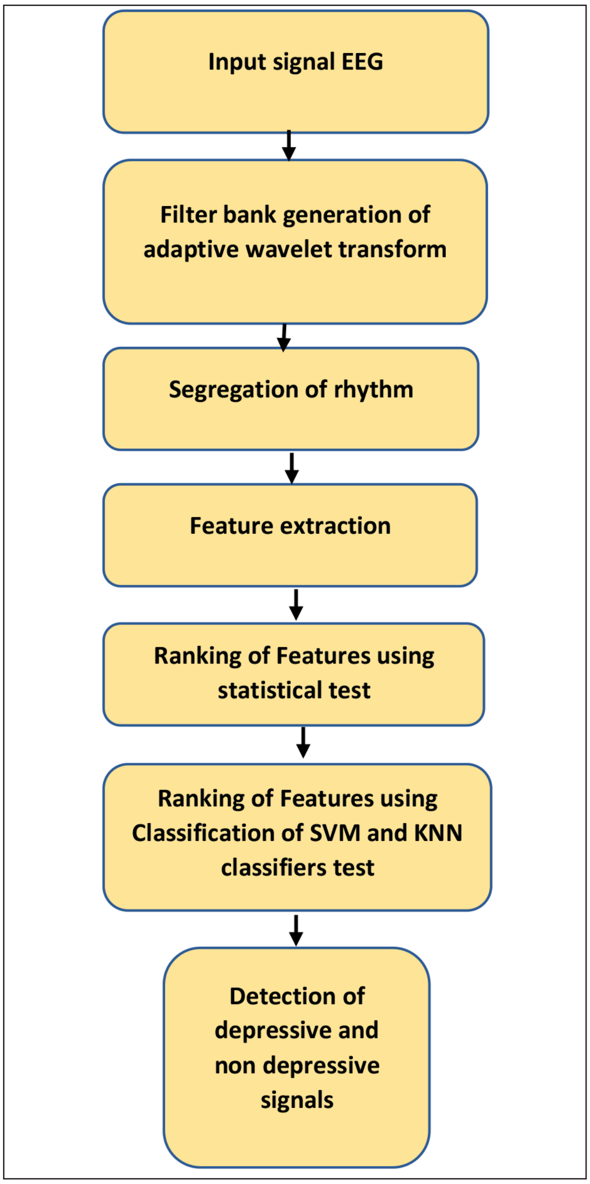

Figure 3. Flow diagram of the proposed method.

gram signals. The spectrum of the EEG signal is taken for this purpose. The signal is then segmented according to the frequency bandwidths of the rhythms, namely delta (δ), theta (θ), alpha (α), beta (β), and gamma (γ). The cut-off frequencies are chosen as 4, 8, 13, 30 and 60. The boundaries of the frequency bandwidth of the different rhythms are tabulated in Table VI.

The γ value was considered to be 0.2367 to minimize the mixing of modes and, at the same time, to avoid the overlapping of the subbands. The more accurately the rhythm signals are extracted, the less the aliasing will be. Information that is greater than sixty hertz is considered to be unwanted.

Feature extraction

The extraction of features is done using the chronotropic-centered technique. This factor is employed to measure the correlation in the domain that is non-linear. It is illustrated by the following equations (2), (3) and (4).

(2)

$$U[k]=\frac{1}{M-K+1}\sum_{m=k}^{M}K_{\mu}(y(m)-y(m-k))$$

(3)

$$U[k]=\frac{1}{M-K+1}\sum_{m=k}^{M}K_{\mu}(y(m)-y(m-k))$$

Here, M is the length of y(m), K is the delay parameter, is the correntropy function and is the kernel function of the Gaussian distribution with the bandwidth .

Correntropy can be computed from the following equation (4).

(4)

$$C_k = U[k]-\widehat{U}[k]$$

Best results were obtained by choosing the K value as 2 and by fixing value as 1. Correntropy has been used earlier by other researchers for the detection of alcohol consumption in patients.

An optimized performance evaluation method for Hybrid SVM-KNN classifiers

The classifiers' performance can be categorized into four different categories. They are Positive True (P_T), Negative True (N_T), Positive False (P_F), and Negative False (N_F). Positive true

Table VI. Frequency bandwidth boundaries of signal rhythms.

Signal rhythm	Boundaries of frequency bandwidth
Delta	0-4
Theta	4-8
Alpha	8-13
Beta	13-30
Gamma	30-60

denotes the count of EEG signals that are depressive. Negative True indicates the count of EEG signals that are non-depressive and detected as non-depressive signals[20]. Positive False indicates the count of EEG signals that are non-depressive and detected as non-depressive signals. Negative False indicates the count of EEG signals that are depressive and detected as non-depressive signals. The accuracy of the classifier depends upon its ability to distinguish between depressive and non-depressive signals exactly[21,22]. Sensitivity and specificity are other parameters that help in determining the accuracy, equation (5).

(5)

$$Accuracy = \frac{P_T + N_T}{P_T + N_T + P_F + N_F} \times 100$$

$$Sensitivity = \frac{P_T}{P_T + N_F} \times 100$$

$$Specificity = \frac{N_T}{N_T + P_F} \times 100$$

The coefficient of correlation is given in the following equation (6).

$$Coefficient\ of\ Correlation = \frac{P_T \times N_T - N_F \times P_F}{(P_T + N_F) \times (P_T + P_F) \times (N_T + N_F) \times (N_T + P_F)}$$

Statistical Analysis

Statistical analysis of the data was performed using SPSS 22.0 (IBM Corp., Armonk, NY, USA). Continuous variables, which were normally distributed, are presented as mean ± standard deviation ($\overline{x}$±s), and between-group comparisons were conducted using independent sample *t*-tests. Categorical variables were presented as percentages (%), and differences were assessed using Chi-square tests, with a significance level of $p<0.05$ indicating statistical significance.

Results

Classification Using SVM Model

The SVM model utilized a radial basis function as the kernel function, as it was found to produce better results compared to other available kernel functions. The scaling factor for the radial basis function was set to 0.5 - 1.5. Table VII displays the mean and standard deviation of left-brain EEG signals for both non-depressed individuals and depressed patients. It can be observed that the C_2 correntropy feature of the delta rhythm in the left-brain EEG signal was significantly higher in depressed patients compared to non-depressed individuals ($p<0.05$). Furthermore, the C_2 correntropy feature of the Alpha, Beta, and Gamma rhythms in the left-brain EEG signal was significantly lower in depressed patients compared to non-depressed individuals ($p<0.05$).

Table VIII presents the mean and standard deviation of right brain EEG signals for different rhythms in both non-depressed individuals and depressed patients. It can be observed that the C_2 correntropy feature of the Delta rhythm in the right brain EEG signal was significantly higher in depressed patients compared to non-depressed individuals ($p<0.05$). Additionally, the C_2 Correntropy feature of the alpha and gamma rhythms in the right brain EEG signal was significantly lower in depressed patients compared to non-depressed individuals ($p<0.05$). Moreover, the C_1 correntropy feature of the gamma rhythm in the right brain EEG signal was significantly higher in depressed patients compared to non-depressed individuals ($p<0.05$).

Table VII. Mean and standard deviation from EEG signals of left half of the brain.

Rhythm	Correntropy feature	Non depressed	Depressed
Delta	C_1	0.3816±0.0078	0.3813±0.0046
	C_2	0.1877±0.0856	0.2310±0.0446*
Theta	C_1	0.3661±0.0134	0.3815±0.0054
	C_2	0.1451±0.0601	0.1147±0.0314
Alpha	C_1	0.3601±0.0141	0.3714±0.0041
	C_2	0.1132±0.0421	0.0581±0.0194*
Beta	C_1	0.3660±0.0132	0.3818±0.0026
	C_2	0.0626±0.0250	0.0214±0.0063*
Gamma	C_1	0.2661±0.0531	0.3654±0.0067
	C_2	0.0653±0.0263	0.0243±0.0078*

*Indicates statistical differences compared to non-depressed individuals, with $p<0.05$.

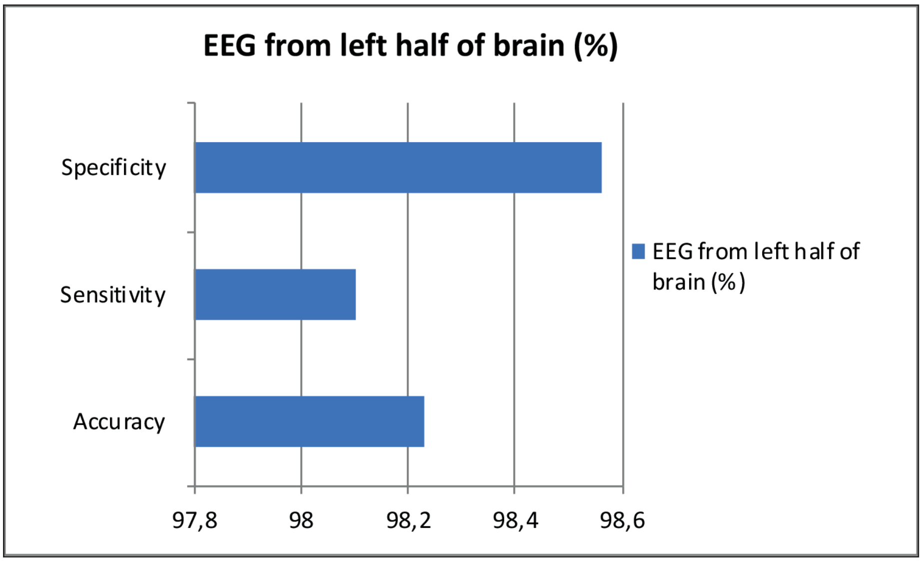

Figure 4. Bar chart representation of SVM classifier results (left hemisphere of brain).

Figures 4 and 5 present the accuracy, sensitivity, and specificity of the EEG signal recognition based on the radial basis function SVM classifier. The SVM classifier achieved an accuracy of 98.23%, sensitivity of 98.10%, and specificity of 98.56% in recognizing left brain EEG signals, with a correlation coefficient of 0.95. In recognizing right brain EEG signals, the SVM classifier achieved an accuracy of 98.74%, sensitivity of 98.43%, and specificity of 99.03%, with a correlation coefficient of 0.96.

Classification Using the KNN Model

The KNN model utilized two types of distance measures, namely the Euclidean distance and the city block distance. The value of k ranged from 2 to 9, specifically $k = 2, 3, 4, ..., 9$. Table IX presents the accuracy, sensitivity, specificity, and correlation coefficient of the KNN model based on the block distance for recognizing left and right brain EEG signals.

Table X shows the parametric results of the KNN classifier with city block distance. The

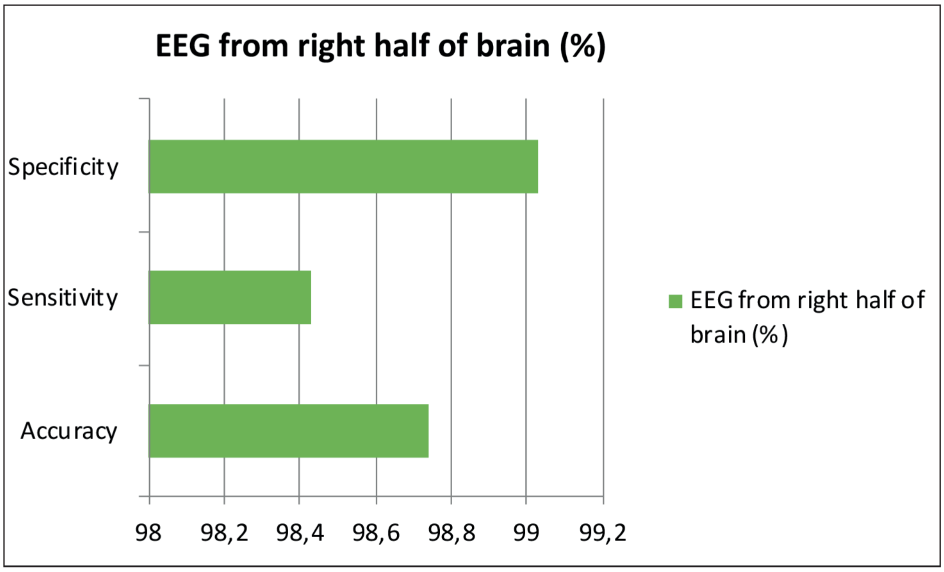

Figure 5. Bar chart representation of SVM classifier results (right hemisphere of brain).

Table VIII. Mean and standard deviation from EEG signals of right half of the brain.

Rhythm	Correntropy feature	Non depressed	Depressed
Delta	C_1	0.3814±0.0076	0.3810±0.0045
	C_2	0.1867±0.0846	0.2312±0.0437*
Theta	C_1	0.3652±0.0133	0.3842±0.0056
	C_2	0.1453±0.0612	0.1151±0.0321
Alpha	C_1	0.3613±0.0138	0.3716±0.0036
	C_2	0.1113±0.0415	0.0578±0.0187
Beta	C_1	0.3659±0.0113	0.3875±0.0032
	C_2	0.0619±0.0247	0.0216±0.0072
Gamma	C_1	0.2652±0.0529	0.3662±0.0075
	C_2	0.0642±0.0278	0.0234±0.0069

*Indicates statistical differences compared to non-depressed individuals, with $p<0.05$.

Table IX. Parametric results of KNN classifier with city block distance.

Parameter	EEG from left half of brain	EEG from right half of brain
Accuracy (%)	97.65	98.36
Sensitivity (%)	96.32	97.35
Specificity (%)	98.82	99.37
Correlation coefficient	0.94	0.95
Count of K	4	6

Electroencephalogram (EEG).

Table X. Parametric results of KNN classifier with Euclidean distance.

Parameter	EEG from left half of brain	EEG from right half of brain
Accuracy (%)	97.42	98.31
Sensitivity (%)	96.14	97.45
Specificity (%)	98.70	99.17
Correlation coefficient	0.94	0.95
Count of K	4	6

Electroencephalogram (EEG), K-Nearest Neighbour (KNN).

KNN classifier based on Euclidean distance exhibited higher accuracy, sensitivity, specificity, and correlation coefficient in recognizing right-brain EEG signals compared to the left-brain.

Classification Using SVM-KNN Model

This study aimed to predict anxiety and depression using ML algorithms. Here, a modified SVM-KNN algorithm was used and for implementing these algorithms the data were collected from the patients who suffered from depression and anxiety. The psychological problems are predicted by the SVM-KNN algorithms. The performance of the improved SVM-KNN algorithm was compared with other algorithms such as Decision Tree[31], Random Forest[32], Naïve bayes[33], Support Vector machine[34], and K-Nearest Neighbour[35] in predicting anxiety and depression. Table XI presents the accuracy, recall, precision, F score, AOC, and Receiver Operation Characteristics (ROC) statistical results for different algorithms in predicting anxiety and depression. The improved SVM-KNN algorithm demonstrated an accuracy of 0.829, recall of 0.811, precision of 0.791, F score of 0.853, AOC of 0.787, and ROC of 0.877 in predicting anxiety. In predicting depression, the improved SVM-KNN algorithm achieved an accuracy of 0.869, recall of 0.842, precision of 0.831, F score of 0.893, AOC of 0.827, and ROC of 0.917. The results indicate that the improved SVM-KNN algorithm outperformed other algorithms in predicting anxiety and depression.

Table XI. Various algorithms used for the prediction of health issues.

Classifier	Illness	Accuracy	Precision	Recall	F score	AOC	ROC
Decision Tree	Anxiety	0.809	0.780	0.771	0.833	0.767	0.857
	Depression	0.728	0.699	0.690	0.752	0.686	0.776
Random Forest	Anxiety	0.797	0.768	0.759	0.821	0.755	0.845
	Depression	0.817	0.788	0.779	0.841	0.775	0.865
Naïve bayes	Anxiety	0.857	0.828	0.819	0.881	0.815	0.905
	Depression	0.908	0.879	0.870	0.932	0.866	0.956
Support Vector machine	Anxiety	0.954	0.925	0.916	0.978	0.912	1.002
	Depression	0.821	0.792	0.783	0.845	0.779	0.869
K-Nearest Neighbour	Anxiety	0.740	0.711	0.702	0.764	0.698	0.788
	Depression	0.809	0.783	0.771	0.833	0.767	0.857
SVM-KNN	Anxiety	0.829	0.811	0.791	0.853	0.787	0.877
	Depression	0.869	0.842	0.831	0.893	0.827	0.917

Area over the curve (AOC), Receiver Operation Characteristics (ROC).

Discussion

The methods employed in this study are based on a SC-RPC trial, which aims to investigate the effect of a low dose of Esketamine on PADS in female patients with systemic tumors. The primary outcome measures are based on the response and follow-up data collected over a one-week treatment period using three questionnaires: PHQ-9, PHQ-15, and MADRS. The psychological assessment, along with the primary outcomes, is analyzed and evaluated by a trained team of two doctors and four nurses who were blinded to the treatment groups. The safety parameters are considered secondary outcome measures to assess the efficiency of the treatment. The SC-RPC trial is designed to explore the efficacy of Esketamine in patients with PADS related to systemic tumors. The findings indicate a significant reduction in post-operative pain during the recovery period and a decrease in negative experiences, providing insights into the potential benefits of Esketamine for this patient population.

The administration of Esketamine significantly reduces symptoms of depression and anxiety. However, the effectiveness of Esketamine in treating depression is somewhat limited. Different dosage variations are explored to address treatment-resistant depression. Safety considerations in the use of Esketamine for PADS treatment encompass monitoring for potential psychiatric side effects. Special attention is required to ensure improved recovery and optimize anesthesia management in this context.

Recent studies[36,37] on Esketamine play a valid role in the reduction of PADS for systemic tumor-affected patients. Initially, the PADS patients with brain tumors had a little bit of refractory depression, and the other is the availability of antidepressants that could be consumed for more than one week of treatment, but the patients who were undergoing such treatment were discharged earlier within one week, and the treatment for PADS is undergone after the discharging process[38]. The SC-RPC is focused on the patients with perioperative health issues and the measures are implemented to improve the prognosis.

The remission rate is determined based on a MADRS score of 20 or less, assessed one week after Esketamine medication. PADS is evaluated using the Hospital Anxiety and Depression Scale (HADS) score, also assessed for one week after medication. A HADS score of less than 11 indicates a higher level of anxiety. Pain levels are monitored during the first four days after surgery, with mean and peak values recorded. Postoperative complications, including psychiatric symptoms, are assessed using a psychiatric rating scale. These complications may involve experiences such as deep sedation, hallucinations, nightmares, and sleep disturbances. The duration of hospital stay is determined within this timeframe.

The support vector machine and the K nearest neighbor classifiers are used to classify the depressed and the non-depressed signals[39]. In the support vector machine classifier, the data set that has to be trained is charted down in a higher dimension space using the kernel function[19]. An optimal hyperplane that is linear classifies the trained data and classifies them. The results showed that the SVM algorithm achieved an accuracy of 0.954, recall of 0.925, precision of 0.916, F score of 0.978, AOC of 0.912, and ROC of 1.002 in predicting anxiety. For predicting depression, the SVM algorithm achieved an accuracy of 0.821, recall of 0.792, precision of 0.783, F score of 0.845, AOC of 0.779, and ROC of 0.869. It can be observed that the SVM algorithm performed well in predicting anxiety, exhibiting high accuracy, recall, and precision. However, in the prediction of depression, although the accuracy was relatively high, the recall and precision were slightly lower compared to anxiety prediction. Further research and adjustment of model parameters are needed to improve the accuracy. K nearest neighbor algorithm is used for faster classification[40]. The measurement of the distance and the number of k neighbors are the two major factors considered for the classification. The results showed that the KNN algorithm achieved an accuracy of 0.740, recall of 0.711, precision of 0.702, F score of 0.764, AOC of 0.698, and ROC of 0.788 in predicting anxiety. For predicting depression, the KNN algorithm achieved an accuracy of 0.809, recall of 0.783, precision of 0.771, F score of 0.833, AOC of 0.767, and ROC of 0.857. The performance of the KNN algorithm in predicting anxiety and depression was moderate. In terms of anxiety prediction, the accuracy and recall were relatively low, indicating lower accuracy and coverage of the model in predicting the anxiety category. In depression prediction, the performance was slightly better, but there was still a certain gap compared to the SVM algorithm. The improved SVM-KNN algorithm, on the other hand, achieved an accuracy of 0.829, recall of 0.811, precision of 0.791, F score of 0.853, AOC of 0.787, and ROC of 0.877 in predicting anxiety. For predicting depression, it achieved an accuracy of 0.869, recall of 0.842, precision of 0.831, F score of 0.893, AOC of 0.827, and ROC of 0.917. These results indicate that the improved SVM-KNN algorithm has good predictive ability for anxiety and depression.

Conclusions

A survey was conducted on 112 female patients with systemic tumors using three questionnaire models: PHQ-9, PHQ-15, and MADRS. Based on SVM and KNN algorithms, an improved SVM-KNN hybrid classifier was established to evaluate the anxiety and depression status of the patients using EEG signals. The results revealed significant differences in brain EEG signals between individuals with and without depression. The improved SVM-KNN algorithm demonstrated good predictive ability for anxiety and depression in this study. These findings provide a valuable reference for the selection and assessment of psychological health intervention strategies for female patients with systemic tumors during the perioperative period. Moreover, they offer reliable evidence and guidance for clinical practice.

Conflict of Interest

The authors declare that there are no conflicts of interest.

Data Availability

The simulation experiment data used to support the findings of this study are available from the corresponding author upon request.

Informed Consent

All the subjects included in this study were aware of the study and signed the informed consent.

Ethics Approval

This research plan has been approved by the Ethics Committee of Yantai Mountain Hospital in Yantai City. Ethical Approval No. 2021028.

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Authors' Contributions

In this study, Chenghai Wang was responsible for assessing perioperative anxiety and depression, Chunyu Lv participated in clinical anesthesia in this study, Yufang Lin participated in data processing and statistical processing in this study, Wenhong Zhang and Xiaoli Tang were responsible for clinical anesthesia in this study, and Luxi Zhao was responsible for project design in this study.

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