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AN INTELLIGENT POSTOPERATIVE CHRONIC PAIN PREDICTION SYSTEM (I-POCPP)

AMELİYAT SONRASI KRONİK AĞRIDA AKILLI BİR ÖNGÖRÜ SİSTEMİ (I-POCPP)

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ABSTRACT

Objective: Postoperative Chronic Pain (POCP) affects the quality of patients' lives. Machine learning and its applications provide significant contributions to pain research. The aim of this study is to predict the POCP status of patients based on perioperative data by developing an "Intelligent POCP Prediction System (I-POCPP)" using the best performing machine learning algorithm.

Material and Method: The dataset for this multi-centered study was collected from 5 tertiary hospitals in Turkey and included 733 patients who had undergone elective surgeries attended by an anesthesiologist in the operating room. Several machine learning prediction algorithms were used. POCP status of the patients diagnosed by the anesthesiologists and the prediction results of the models were compared to evaluate the performance of the models.

Results: It was found that the k-Nearest Neighbour (kNN), Random Forest (RF), and C5.0 models were able to predict the POCP status of a patient with an accuracy higher than 80%. The performance of RF was considered, while the kNN algorithm has no stable model. According to RF and Classification and Regression Tree (CART) algorithms' attribute importance ranking, "Incision site", "Age", and "Primary diagnosis for operation" are common attributes. Since the attribute importance ranking obtained as a result of the C5.0 algorithm was not consistent with the RF and CART models, the results of this model were not evaluated. The best result among all models was obtained by RF, and I-POCPP has been developed accordingly.

ÖZET

Amaç: Ameliyat Sonrası Kronik Ağrı (*Postoperative Chronic Pain - POCP*), hastaların yaşam kalitesini etkilemektedir. Makine öğrenmesi ve uygulamaları, ağrı araştırmalarına önemli katkılar sağlamaktadır. En iyi performans gösteren makine öğrenmesi algoritmasını kullanarak "Ameliyat Sonrası Kronik Ağrıda Akıllı Bir Öngörü Sistemi (I-POCPP)" geliştirerek perioperatif verilere dayalı olarak hastaların ameliyat sonrası kronik ağrı durumunu öngörmek hedeflenmiştir.

Gereç ve Yöntem: Bu çok merkezli çalışmanın veri seti, Türkiye'deki üçüncü basamak 5 hastanede elektif koşullarda anestezi altında ameliyat olan 733 hastadan toplanmıştır. Çalışmada farklı makine öğrenmesi öngörü algoritmaları kullanılmıştır. Anestezistler tarafından tanı konulan hastaların gerçekleşen kronik ağrı durumu ve modellerin öngörü sonuçları karşılaştırılarak modellerin performansı değerlendirilmiştir.

Bulgular: k-En Yakın Komşu (kNN), Rastgele Orman (RF) ve C5.0 modellerinin bir hastanın ameliyat sonrası kronik ağrı durumunu %80'den yüksek doğrulukla öngörebildiği bulunmuştur. kNN algoritmasının kararlı bir modeli olmadığı düşüncesiyle RF performansı dikkate alınmıştır. RF ve Sınıflandırma ve Regresyon Ağacı (CART) algoritmalarının nitelik önem sıralamasına göre "Kesi yeri", "Yaş" ve "Ameliyat nedeni" ortaktır. C5.0 algoritması sonucunda elde edilen nitelik önem sıralaması RF ve CART modelleri ile uyumlu olmadığı için bu modelin sonuçları değerlendirilmemiştir. Tüm modeller arasında en iyi sonuç RF ile elde edilmiştir ve buna göre I-POCPP geliştirilmiştir.

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Conclusion: Fast, accurate, and efficient treatment of POCP provided by I-POCPP could allow the patient to return to daily life earlier.

Keywords: Postoperative Chronic Pain, Machine Learning, Classification, Decision Support System

Sonuç: I-POCPP sistemiyle sağlanan ameliyat sonrası kronik ağrının hızlı, doğru ve etkin tedavisi, hastanın günlük yaşama daha erken dönmesini sağlayabilir.

Anahtar Kelimeler: Ameliyat Sonrası Kronik Ağrı, Makine Öğrenmesi, Sınıflandırma, Karar Destek Sistemi

INTRODUCTION

Postoperative Chronic (or persistent) Pain (POCP) is defined as pain developing after surgery, with a duration of at least two months and is not related to pre-existing problems and other reasons are excluded. Postoperative pain incidence has been reported as 10%-60% in several studies. Generally, type of surgery (amputations, thoracotomies, cardiac surgery, and breast surgery), presence of preoperative pain, psychological status (anxiety, depression), young age and female gender, surgical technique (open surgery, surgery duration >3 hours), and the severe acute postoperative pain are related with higher incidence (1, 2). The implementation of preventive measures by predicting the possibility of developing chronic pain will raise the quality of patients' lives and prevent severe labor and economic losses. Multidisciplinary methods are used to overcome the problems mentioned in chronic pain management. As a part of artificial intelligence, machine learning has attracted increasing interest, and it is being used in many fields such as pain research (3). Predicting postoperative pain before surgery is of utmost importance for pain prevention. The machine learning algorithms are numerous. The k-Nearest Neighbor Algorithm (kNN), Naïve Bayes Classifier (NB), Classification and Regression Tree (CART), C5.0, Random Forest (RF), and Artificial Neural Networks (ANNs) are frequently used currently.

This study's primary aim is to find out the best machine learning algorithm for predicting POCP based on the perioperative data. Moreover, clinical data obtained and the developed Intelligent POCP Prediction System (I-POCPP) are presented.

MATERIAL AND METHODS

A prospective longitudinal study written consent was obtained from the participating hospitals and patients. The CRoss-Industry Standard Process for Data Mining (CRISP-DM) steps were followed (4, 5). Since the introduction part covers the business (problem) understanding, this section starts with the data understanding step of CRISP-DM.

Data Understanding

Following informed consent, the data of 1027 patients who had undergone surgery in elective conditions attended by an anesthesiologist in the operating room, were collected from 5 tertiary hospitals in Istanbul and Izmir (all surgical departments of Istanbul University-Cerrahpaşa Medical Faculty and Institute of Cardiology, Izmir Tepecik Training and Research Hospital, Istanbul Training and Research Hospital, and Bezmialem Vakif University Faculty of Medicine and Umraniye Training and Research Hospital) by the ASK study group (see Acknowledgements) between March 2016 and December 2017. The questionnaire developed by Sutas Bozkurt et al. (6) consisted of 35 variables, and the answers provided by the patients and anesthesiologists in charge were recorded. Thirty-four of the variables are predictive attributes, and one of them is the target attribute (condition) which indicates the patient's POCP status (Table 1).

Between March 2016 and December 2017, the patients who had undergone surgery were called every two weeks to maintain good communication for up to 2 months, and VAS scores were recorded by the ASK group. The patients who reported pain at the end of 2 months were revisited and received pain consultation from the team. Two hundred and thirty patients were excluded from the dataset. Of these, 208 of them gave up follow-up, and 22 of them had been reoperated on during the follow-up period. Sixty-four observations were excluded due to the missing values and two of these patients had developed POCP. Finally, the data of 733 patients formed the dataset, of which 144 had developed POCP in the two-month follow-up period. The inclusion criteria were age above 18, elective surgery, and patients who had undergone repeated procedures. Reoperations were excluded.

The attributes used in this study are listed (Table 1). Some information about these attributes is summarized below:

- Forty-three percent of the patients were male, and 57% were female.
- All patients were above 18 years old, and the eldest was 84 years old (45.5 mean, +/- 15.44 standard deviation, 44 median).
- Almost one-third of the patients were smokers, alcohol abusers were very rare, and there were no drug abusers.
- Only 6-7% incidence was observed for each variable: people living alone, poor economic status, high preoperative anxiety, and admission rate to intensive care unit postoperatively.

Table 1: Attributes of POCP dataset

Predictive Attributes related to Patient's Demography		**Predictive Attributes related to Preoperative History**	**Predictive Attributes related to Anesthesia**	**Predictive Attributes related to Operation**
Lifestyle (single, married, with family, living alone)	Alcohol abuse	Count of operations (from a different site)	Anesthesia technique (general, regional, etc.)	The primary diagnosis for operation
Age (years)	Smoking (packs/ day)	Count of operations (from the same site)	Intraoperative-opioid	Hospital stay (days, ICU admission)
Geographical region in Turkey (Marmara, Aegean, Eastern Anatolia, etc.)	Smoking (for ... years)	Preoperative pain status	Postoperative acute pain treatment (NSAID)	Operation style (open, laparoscopic, endoscopic etc.)
Turkish citizen/ Foreigner (born and live in Turkey /immigrant or foreign residence)	Presence of Systemic disease (cardiac, renal, respiratory, etc.)	Preoperative pain syndrome	Postoperative. acute pain treatment (opioid)	Incision (site)
Appearance (normal, cachectic, obese)	Analgesics routinely used	Preoperative anxiety evaluated by an anesthesiologist	Postoperative acute pain treatment (LA)	Position (supine, prone, trendelenburg, sitting etc.)
ASA (I, II, III)	Continuous medications		Postoperative acute pain treatment (Infiltration of the incision site)	Duration of operation (min.)
Gender	Socio-economic status (poor, midlevel income, rich)		Postoperative acute pain treatment (other)	Use of electrocautery
Smoking				
Target Attribute				
Patient's POCP Status (whether POCP (1) or not POCP (0))				

ASA:American Society of Anesthesiologists risk scoring, LA: Local anesthetic, NSAID: Nonsteroid antianalgesic drug

- The study group mainly consisted of Turkish citizens of different ethnicity, and 14% were immigrants from various countries of the Middle East or Caucasians, living in Turkey with a residence permit, thus representing the unique nature of Turkey.
- 58.39% of the patients had a body mass index (BMI) higher than 25, and only 2.45% of the patients were cachectic.
- The incidence of ASA I, II, and III were 52.11%, 41.34%, and 6.55%, respectively.
- The anesthesia techniques were general anesthesia, combined (general and regional anesthesia), regional anesthesia with sedation, and sedoanalgesia, 67.12%, 2.59%, 27.83%, and 2.46%, respectively.
- The data collected from all types of surgical disciplines included all parts of the body. The reason for surgery on the body because of several malignancies was 15.14%. Cesarean section was the most frequent procedure (14.6% of all cases), followed by orthopedic procedures 13.37% and cardiac surgery 4.1%, and all types of surgeries on the head, neck, and trunk were performed.
- The incision size was less than 10 cm in 48.84%, more than 10 cm in 24.28% of patients, and 14.46% had laparoscopic, and 12.42% had endoscopic procedures.
- POCP was reported by 144 patients and of these 7.64% (n=11) complained of severe pain (VAS>7), 24.30% (n=35) moderate pain (VAS 5-7) and mild pain 68.06% (n=98).

Data preparation

The missing value imputation was performed by consulting anesthesiologists in five hospitals. The dataset being normalized with min-max normalization technique enabled a scale of the attributes between 0 and 1. Also, over-sampling and under-sampling methods were applied to the initial dataset to improve the results. Over-sampling aimed to increase the number of observations that belonged to the minority class of the target attribute, and under-sampling aimed to decrease the number of observations that belonged to the majority class of the target attribute (7).

Modeling

The research problem of this study was considered a prediction problem. Therefore, the following supervised machine learning techniques were used: k-Nearest Neighbor Algorithm (kNN) (with Gower and Euclidean distances), Naïve Bayes Classifier (NB), Classification and Regression Tree (CART), C5.0, Random Forest (RF) and Artificial Neural Networks (ANNs) (with Backpropagation Algorithm). Here, different algorithms can be considered as the categories of the index test. The actual POCP status of the patients was used as a reference (gold) standard to evaluate the performance of the algorithms.

For the analyses in the modeling step, R programming language and RStudio were used (8,9). 5-fold cross-validation was used as a performance evaluation technique. The evaluation step of the CRISP-DM is included in the Results section of this study. For performance evaluation, accuracy, sensitivity, specificity, positive predictive value, negative predictive value, and F1 Score metrics were calculated for each model. These metrics were ordered by F1 Score and accuracy, respectively.

RESULTS

Performance evaluation results

In this section, at first, the top five model performance evaluation metrics obtained from the initial dataset, over-sampling dataset, and under-sampling dataset are given respectively (Table 2, Table 3, and Table 4). kNN

Table 2: Performance evaluation metrics of the initial dataset (without sampling)

Accuracy	Sensitivity	Specificity	PPV	NPV	F1	Method	Distance	k
0.823	0.257	0.961	0.661	0.841	0.360	kNN	Euclidean	7
0.820	0.209	0.969	0.662	0.834	0.310	kNN	Euclidean	11
0.820	0.173	0.978	0.672	0.829	0.274	RF	—	—
0.819	0.202	0.969	0.646	0.832	0.303	kNN	Euclidean	13
0.817	0.188	0.971	0.629	0.830	0.287	kNN	Euclidean	14

PPV: positive predictive value, NPV: negative predictive value, F1: F1 Score, k: parameter of kNN algorithm.

Table 3: Performance evaluation metrics of over-sampling dataset

Accuracy	Sensitivity	Specificity	PPV	NPV	F1	Method	k	hidden1	hidden2
0.812	0.215	0.958	0.542	0.833	0.304	RF	—	—	—
0.763	0.340	0.866	0.386	0.843	0.360	kNN (Gower)	2	—	—
0.756	0.312	0.864	0.367	0.837	0.333	ANN	—	200	2
0.755	0.243	0.880	0.355	0.826	0.284	ANN	—	250	2
0.754	0.312	0.863	0.361	0.837	0.333	ANN	—	100	—

PPV: positive predictive value, NPV; negative predictive value, F1: F1 Score, k: parameter of kNN algorithm. hidden1 and hidden 2: neuron numbers of the hidden layers of the ANN.

Table 4: Performance evaluation metrics of under-sampling dataset

Accuracy	Sensitivity	Specificity	PPV	NPV	F1	Method	Distance	k
0.742	0.403	0.825	0.366	0.849	0.383	kNN	Gower	14
0.742	0.368	0.834	0.368	0.843	0.363	kNN	Gower	20
0.738	0.375	0.827	0.349	0.844	0.360	kNN	Gower	18
0.730	0.383	0.815	0.335	0.844	0.356	kNN	Gower	16
0.724	0.375	0.810	0.326	0.841	0.348	kNN	Gower	6

PPV; positive predictive value, NPV; negative predictive value, F1: F1 Score, k: parameter of kNN algorithm.

Table 5: Performance evaluation metrics in terms of algorithms

Accuracy	Sensitivity	Specificity	PPV	NPV	F1	Method	k	hidden1
0.823	0.257	0.961	0.661	0.841	0.360	kNN (Euclidean)	7	—
0.820	0.173	0.978	0.672	0.829	0.274	RF	—	—
0.817	0.187	0.971	0.635	0.830	0.285	kNN (Gower)	11	—
0.809	0.173	0.964	0.530	0.827	0.253	C5.0	—	—
0.793	0.209	0.935	0.509	0.829	0.277	CART	—	—
0.786	0.241	0.886	0.340	0.813	0.282	ANN	—	500
0.764	0.389	0.856	0.405	0.852	0.393	NB	—	—

PPV: positive predictive value, NPV: negative predictive value, F1: F1 Score, k: parameter of kNN algorithm, hidden1: neuron number of the hidden layer of the ANN.

(with Euclidean distance) models had the highest accuracy values of the models for the initial dataset (Table 2). The kNN model was able to predict a patient's POCP status with 82.3% accuracy according to only the seven nearest observations in the given training dataset (Table 2). It can be seen that there was no such big difference between the best kNN model and the RF model (accuracy difference was only 0.3%).

The results of over-sampling and under-sampling trials were lower than the results of the analyses on the initial dataset (Table 2, Table 3, and Table 4). While the RF model was first in the over-sampling dataset (acc=81.2%), kNN models were first in the under-sampling dataset.

The general results of model performance showed the highest accuracy of each algorithm. kNN (Euclidean and Gower distances), RF, and C5.0 models were able to predict the POCP status of a patient with an accuracy higher than 80% (Table 5). Since the kNN algorithm has no stable model, in other words, it predicts to an unlabeled/a new observations' POCP status each time, all distances between the unlabeled observation and observations in the training dataset should be calculated. In this study, the RF model with the highest accuracy (82%) was chosen as the best model to predict a patient's POCP status.

The most important attributes among the POCP indicators

Considering the highest performance results of the decision tree algorithms used in this study (RF, C5.0, and CART), attributes of the POCP dataset were ordered according to their effect on the final decision about the patient's POCP status. The order of the attribute importance according to the RF, C5.0, and CART models are given (Table 6).

· The top five attributes according to the C5.0 model were "Postoperative acute pain local anesthesia (trunk or peripheral or central blocks with the use of local anesthetics (LA))", "Postoperative acute pain treatment with other than LA, NSAID or opioids (other)", "Postoperative acute pain treatment with non-steroid anti-inflammatory drugs (NSAID)", "Smoking", and "Turkish citizen/Foreigner".

Since the attribute importance ranking obtained as a result of C5.0 algorithm was not consistent with the RF and CART models, the results of this model were not evaluated.

· The top five attributes according to the RF model were "Incision site", "Age", "Geographical Region in Turkey", "Primary diagnosis for operation", and "Duration of operation (min.)".
· The top five attributes according to the CART model were "Incision site", "Primary diagnosis for operation", "Anesthesia technique", "Postoperative acute pain (LA)", and "Age".
· The intersection of the results of these two algorithms were "Incision site", "Age", and "Primary diagnosis for operation".

Several rules that were obtained by the CART model are given (Figure 1):

· IF INCISION is Foot or Leg or Lumbar AND GEOGRAPHICAL REGION is Eastern Anatolia or Aegean or Marmara or Overseas AND AGE is lower than 64 THEN POCP Status of the Patient is NEGATIVE (75.6%).
· IF INCISION is Foot or Leg or Lumbar AND GEOGRAPHICAL REGION is Eastern Anatolia or Aegean or Marmara or Overseas AND AGE is greater than or equal to 64 THEN POCP Status of the Patient is POSITIVE (33.2%).

Deployment: Development of intelligent POCP prediction system (I-POCPP)

As the final step of the CRISP-DM, an Intelligent POCP Prediction System (I-POCPP) was developed by using the RF model to predict the POCP status of a patient before the surgery in the previous section. This system was de-

Table 6: The importance of the attributes in terms of decision tree algorithms

Attribute	RF	C5.0	CART
Incision	19.148	0	27.058
Age	16.832	0	9.018
Geographical region in Turkey	14.604	0	7.539
The primary diagnosis for operation	13.500	0	21.842
Duration of operation (min.)	11.640	0	1.333
Count of operations (from the different site)	8.826	0	5.349
Anesthesia technique	6.844	0	13.074
Gender	6.756	0	1.652
Operation style	5.939	3.240	7.091
Smoking (for … years)	5.834	0	2.167
Preoperative anxiety evaluated by an anesthesiologist	4.709	0	0
Postoperative. acute pain treatment (LA)	4.569	100	12.820
Socio-economic status	4.529	1.700	0
ASA	4.121	0	0
Analgesics routinely used	4.068	0	2.057
Smoking (packs/day)	3.952	0	3.391
Preoperative pain syndrome	3.422	3.070	0
Position	3.418	0	0
Count of operations (from the same site)	3.283	0	3.223
Appearance	3.248	0	1.258
Hospital stay	3.107	0	0
Preoperative pain status	2.989	0	8.259
Intraoperative-opioid	2.683	0	1.327
Continuous medications	2.610	0	1.212
Postoperative acute pain (opioid)	2.470	0	0
Turkish citizen/Foreigner	2.305	5.960	0
Use of electrocautery	2.296	0	0
Lifestyle	2.280	0	0
Presence of systemic disease	2.250	0	0
Smoking	2.064	9.200	3.391
Alcohol	1.883	0	0
Postoperative acute pain (other)	1.767	89.440	0
Postoperative acute pain (NSAID)	1.508	10.560	0
Postoperative acute pain (infiltration of the incision site)	0.355	0	0

ASA: American Society of Anesthesiologists risk scoring, LA: Local anesthetic, NSAID: Nonsteroid antianalgesic drug.

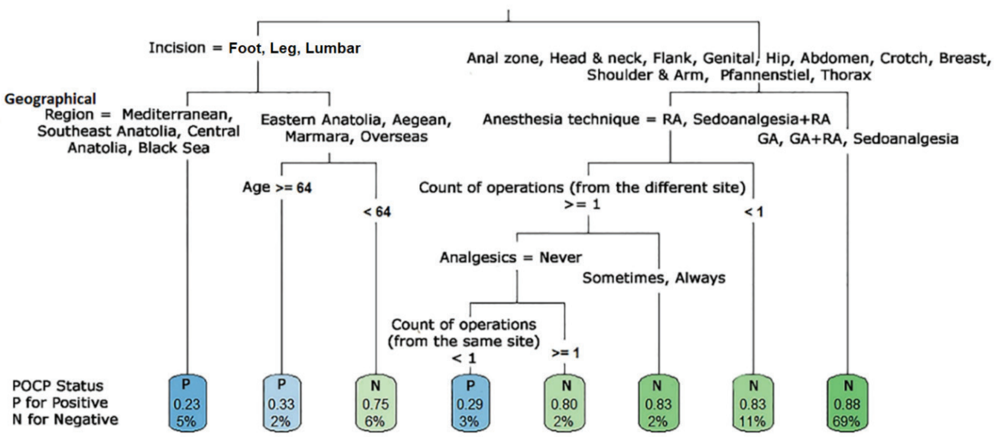

Figure 1: Decision tree of the CART model (GA; General Anesthesia, RA; Regional Anesthesia)

veloped using shiny and shinyapps.io and is easily accessible from the web and mobile with the following link: https://zekiozen.shinyapps.io/pocp/ (10, 11). Surgeons can select the best answer to each POCP indicator for a patient on four different tabs, namely Demography, Preoperative History, Anesthesia History, and Operation. "Next" and "Previous" buttons can be used to make any necessary changes to the form. After the data input process is finalized and the "Predict!" button is clicked, the patient's POCP status appears as POSITIVE or NEGATIVE.

DISCUSSION

In recent years, the technological development of computer science has provided solutions for problems in medicine. Artificial intelligence, robotics, deep learning, and data mining are used to develop computer-aided diagnosis and treatment systems. One of the most popular branches of artificial intelligence is machine learning. Today, machine learning can be applied to many different domains with the help of developments in computing technology, data storage, and data processing (12). Basically, machine learning aims to develop systems with the help of various techniques that use data as experience.

In the literature, several studies emphasize the importance of predicting postoperative pain; however, machine learning methods were not used in any of these studies, which were conducted mostly by medical staff, (13-16). It has been stated that contemporary computer-based tools and machine learning algorithms can help to understand pain-related data and contribute to the studies and treatments of pain (3).

Tighe et al. have established models based on machine learning techniques to identify patients with preoperative risk of chronic pain for preventive treatment (17). The dataset used for analysis includes demographic and surgical records of 9860 patients who were operated on for six months. It was seen that the models were successful in line with the purpose of the study, and more successful results were obtained with the use of size reduction techniques in the dataset. In addition to different algorithms, C4.5 and RF were used (17). In our study, although C5.0, which is the improved version of the C4.5 algorithm, was used, obtained results from this algorithm are not promising. It can be said that not every result obtained from different machine learning models is directly usable by physicians. Supporting these results with an expert opinion can provide much better results. Nickerson et al. carried out a study using predictive machine learning algorithms to perform the correct analgesic medication and avoid unnecessary side effects of drugs during the postoperative chronic pain treatment (18). This study aimed to determine the significance level of predictive features with RF. The results show that machine learning techniques are important in developing strategies against postoperative pain. In the study conducted by Garcia-Chimeno et al. to estimate migraine pain by machine learning techniques, RF was used to determine the best predictive features (19). It was determined that when the analysis was used, selected classifiers were more successful. Demographic data, anxiety depression test results, and measured migraine pain values of 52 people were used in the data analysis. In a study conducted by Lötsch et al., machine learning techniques were used to establish shorter, non-exhaustive questionnaires instead of long and repetitive questionnaires which might affect the psychology of the patient to whom it was applied to predetermine the chronic pain and take the necessary precautions (20). With RF, the importance of the features in the previous questionnaires was determined, and a short survey was obtained based on essential features. The short questionnaire was found to be successful in predicting chronic pain. The data of 1000 female patients who had undergone surgery were included in the study and were followed up for three years after surgery.

NB is a popular algorithm that is used in cancer classification and bioinformatics studies (21, 22). CART is another popular algorithm to predict the risk of patients with pulmonary disease and breast cancer classification (23, 24). ANNs are used in some POCP research. Salgueiro et al. performed ANNs using clinical variables to predict the response of persons with fibromyalgia syndrome (FMS) to a standard, 4-weeks interdisciplinary pain program (25). ANNs are used to predict persistent facial pain in patients operated on for chronic rhinosinusitis (26). Tighe et al. applied five machine learning algorithms, including ANNs, to their dataset, consisting of 8071 surgical patients using 796 clinical variables, to predict postoperative pain outcomes in a retrospective cohort (27). In another study, Tighe et al. used multilayer neural networks and other machine learning classifiers to predict patients requiring a postoperative femoral nerve block (28).

In this study, the authors aimed to develop an Intelligent Postoperative Chronic Pain Prediction System (I-POCPP), which supports the surgical team's decision to choose the appropriate anesthesia method for the surgery and determine a more accurate diagnosis and treatment methods for potential POCP patients.

The importance of this study can be explained with the following aspects:

- There is no such study in the literature about predicting POCP with an intelligent system. Since the system is unique, it is believed that I-POCPP is beneficial for the team. Furthermore, various studies have shown that machine learning techniques are used for pain prediction; however, an intelligent system has not been developed (3).

- The most important indicators of POCP are determined by using different machine learning classification algorithms. These indicators are "Incision site", "Age", and "Geographical Region" (geographical regions in Turkey) according to the RF algorithm's attribute importance order. The previous study by Sutas Bozkurt et al. shows that while socio-economic status, appearance, and preoperative pain status had no effect on the potential development of POCP, older age played a major role in the development of POCP (6). Therefore, the results of both studies are consistent in terms of these indicators.
- Order of indicators changes in terms of RF and CART algorithms. These results may help the surgical team to make decisions about the patient's POCP status before any kind of surgery if they combine the most important indicators determined by the algorithms with their expertise and experience. Also, the decision-making process will be easier and faster for physicians, and they can ignore indicators with a low importance level.
- The I-POCPP is easy to use and simply accessible from the web and mobile with its URL (https://zekiozen.shinyapps.io/pocp/). It provides prediction opportunities for POCP without time and place constraints.
- The results also showed that by using I-POCPP, physicians will not have to wait for 60 days (within 15 days periods) after the surgery to observe whether POCP will develop. The system provides an early POCP prediction opportunity for physicians. Moreover, the system will support the surgical team's decision to choose the appropriate anesthesia method for the surgery and determine a more accurate diagnosis and treatment methods for potential POCP patients.
- From the financial perspective, early diagnosis and treatment of POCP provided by I-POCPP may reduce the workload of the algology clinics in the long term. From the patient's perspective, fast, accurate, and efficient treatment of POCP could allow the patient to return to daily life earlier.

In this study, only 144 of the 733 patients had POCP. This can be considered as the only limitation of the study because, from the supervised learning perspective, it is hard to make good predictions with the imbalanced data. In this case, there is a possibility to obtain unreal high accuracy results from the prediction models. Therefore, under-sampling and over-sampling methods were employed in the data pre-processing stage to balance the ratio of POCP status. The results did not show any significant improvement. Moreover, different advanced machine learning techniques such as extreme learning machines, deep learning, support vector machines, etc., and different performance evaluation methods such as hold-out, leave-one-out cross-validation, bootstrap, etc., can be used in the future studies. Data may be collected from various centers with national and international collaborations, so more generalized results can be obtained.

CONCLUSIONS

I-POCPP provides an early POCP prediction opportunity for physicians. By using I-POCPP, physicians will not have to wait for the two months follow-up period after the surgery to observe whether POCP will develop. Moreover, the system will support the surgical team's decisions on choosing the appropriate anesthesia and surgery method, determining a more accurate diagnosis and treatment methods for potential POCP patients. Fast, accurate, and efficient treatment of POCP provided by I-POCPP could allow the patient to return to daily life earlier.

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