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Artificial intelligence in perioperative pain management: A review

Yan Liao[1*], Zhanheng Chen[1*],Wangzheqi Zhang[1*], Lindong Cheng[2], Yanchen Lin[2], Ping Li[3], Miao Zhou[4], Mi Li[1], ChunHua Liao[1]

[1]School of Anesthesiology, Naval Medical University, Shanghai 200433, China. [2]Graduate School, Hebei North University, Zhangjiakou 075000, China. [3]Graduate School, Wannan Medical College, Wuhu 241000, China. [4]Department of Anesthesiology, the Affiliated Cancer Hospital of Nanjing Medical University, Jiangsu Cancer Hospital, Jiangsu Institute of Cancer Research, Nanjing Medical University, Nanjing 210009, China.
[*]The authors contribute equally.

Corresponding authors: Miao Zhou, Mi Li and ChunHua Liao.

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Highlights

- Artificial intelligence (AI) is lauded for its capacity to resolve intricate problems with unwavering efficiency, devoid of fatigue. To elucidate the potential of AI in perioperative pain management, we have meticulously surveyed a vast array of scholarly works to discern the landscape of research in this multifaceted domain.
- Conventional perioperative pain studies have primarily confined their scope to clinical aspects. However, this re view delves into the amalgamation of AI and perioperative pain, heralding a diverse methodology for pain control.
- AI's applicability in medical domains, particularly anesthesia, has spawned numerous inquiries into its synergy with perioperative pain. Yet, a dearth of comprehensive reviews encapsulating the current research milieu, pin pointing hurdles, and envisioning future directions in this sphere necessitated the present discourse.
- We herein offer horizontal and vertical assessments of diverse models and algorithms employed in periopera tive pain management, encapsulated in diagrammatic form for reader accessibility. The compilation of this re view draws from a spectrum of online scholarly repositories, thus ensuring a thorough and relevant assembly of insights.

Abstract

Artificial intelligence (AI) leverages its swift, precise, and fatigue-resistant problem-solving abilities to significantly influence anesthetic practices, ranging from monitoring the depth of anesthesia to controlling its delivery and predicting events. Within the domain of anesthesia, pain management plays a pivotal role. This review examines the promises and challenges of integrating AI into perioperative pain management, offering an in-depth analysis of their converging interfaces. Given the breadth of research in perioperative pain management, the review centers on the quality of training datasets, the integrity of experimental outcomes, and the diversity of algorithmic approaches. We conducted a thorough examination of studies from electronic databases, grouping them into three core themes: pain assessment, therapeutic interventions, and the forecasting of pain management-related adverse effects. Subsequently, we addressed the limitations of AI application, such as the need for enhanced predic-

Address correspondence to: Miao Zhou, The Affiliated Cancer Hospital of Nanjing Medical University, Department of Anesthesiology, Jiangsu Cancer Hospital, Jiangsu Institute of Cancer Research, Nanjing Medical University, Nanjing 210009, China. E-mail: zhoumiao2613@163.com; Tel: +86 18217567295. **Mi Li**, School of Anesthesiology, Naval Medical University, 800 Xiangyin Road, Yangpu District, Shanghai 200433, China. E-mail: limi@smmu.edu.cn; Tel: +86-21-81872033. **Chunhua Liao**, School of Anesthesiology, Naval Medical University, 800 Xiangyin Road, Yangpu District. Shanghai 200433, China. E-mail: Liaochh7@smmu.edu.cn; Tel: +86 21 81872025.

tive accuracy, privacy concerns, and the development of a robust database. Building upon these considerations, we propose avenues for future research that harness the potential of AI to effectively contribute to perioperative pain management, aiming to refine the clinical utility of this technology.

Keywords: Artificial intelligence, pain management, perioperative pain, acute pain

Introduction

Artificial intelligence (AI)

AI is characterized by the "science and engineering of creating intelligent machines," as conceptualized in prior research. In 1950, the seminal work of Alan Turing, a mathematician and AI's progenitor, proposed the notion of machines emulating human cognitive processes [1]. Over the past several decades, AI has burgeoned into a multifaceted discipline, encompassing specialized areas such as machine learning, deep learning, neural networks, computer vision, among others [1, 2]. Numerous taxonomies have been proposed to categorize AI. Primordially, AI is bifurcated into Artificial Narrow Intelligence, which predominates in specific domains, Artificial General Intelligence, which approximates human-level intelligence, and Artificial Superintelligence, which surpasses human capabilities by fostering innovation and social interaction [3].

The advent of advanced technology has propelled AI into a multitude of sectors, including robotics, natural language processing, simulation, learning systems, problem-solving methodologies, and gaming. As depicted in **Figure 1**, each of these sectors is further subdivided into a tapestry of specialized fields, reflecting the intricate taxonomy that arises from AI's diverse applications [4]. Machine learning, a subset of AI algorithms, is particularly adept at addressing challenges through classification and regression techniques, capable of parsing and interpreting diverse data formats, ranging from text and numerical datasets to visual and auditory information [5]. Drawing inspiration from the complexities of the nervous system, deep neural networks represent a class of models that bridge the gap between those informed by the workings of biological neurons and those that delve into the cognitive aspects of human information processing. These intricate networks are capable of processing limited inputs and producing high-quality outputs by efficiently leveraging the scarce data contained within their hidden layers [6]. Computer vision is a critical component of AI, empowering machines with the ability to comprehend and decipher visual information, encompassing images and videos. This field extracts salient features from visual data, such as hue, form, and texture. AI has achieved substantial advancement and is extensively applied across various domains, each with its subset of specializations and areas of emphasis [5].

AI's paramount advantage over human cognition lies in its capacity for predictive analytics when confronting extensive explanatory variables or intricate interdependencies among features. In the face of complex challenges, the human mind can laboriously parse through pertinent experiences, resulting in a taxing process. In contrast, AI leverages data-driven methodologies and extensive datasets, affording it a distinctive edge in managing such complexities. The technology can seamlessly compute the most nuanced computations and tenaciously pursue solutions without fatigue [7]. For instance, AI can encapsulate a multitude of variables, referred to as 'model features,' and thereafter elucidate intricate correlations among these features [8]. Subsequently, AI-based algorithms and models are being implemented across a spectrum of medical disciplines, including anesthesiology. AI is augmenting the oversight of anesthetic depth, forecasting the likelihood of deleterious events throughout anesthesia, supporting ultrasound-guided interventions, and assisting in the prediction and administration of pain phenotypes. Across all these domains, the amalgamation of AI is demonstrating enhanced efficacy when compared to conventional approaches [5, 9].

Perioperative pain management

What is pain? Extensive research on pain has been conducted from perspectives of molecules, cells, etc. [10]. The prevalent conceptualization of pain characterizes it as an "unpleasant sensory and emotional experience linked to real or potential tissue harm, or articulated in terms of such harm [11]." Prevalence of perioperative pain is considerable, particularly in the postoperative phase. Data indicate that roughly half of all surgical patients report moderate to severe pain levels within two weeks post-operation, with over 10% experiencing severe to extreme pain intensity [12]. This phenomenon extends beyond major surgical procedures, being a widespread occurrence across various types of surgery [13]. Effective pain management thus constitutes a critical component of the an-

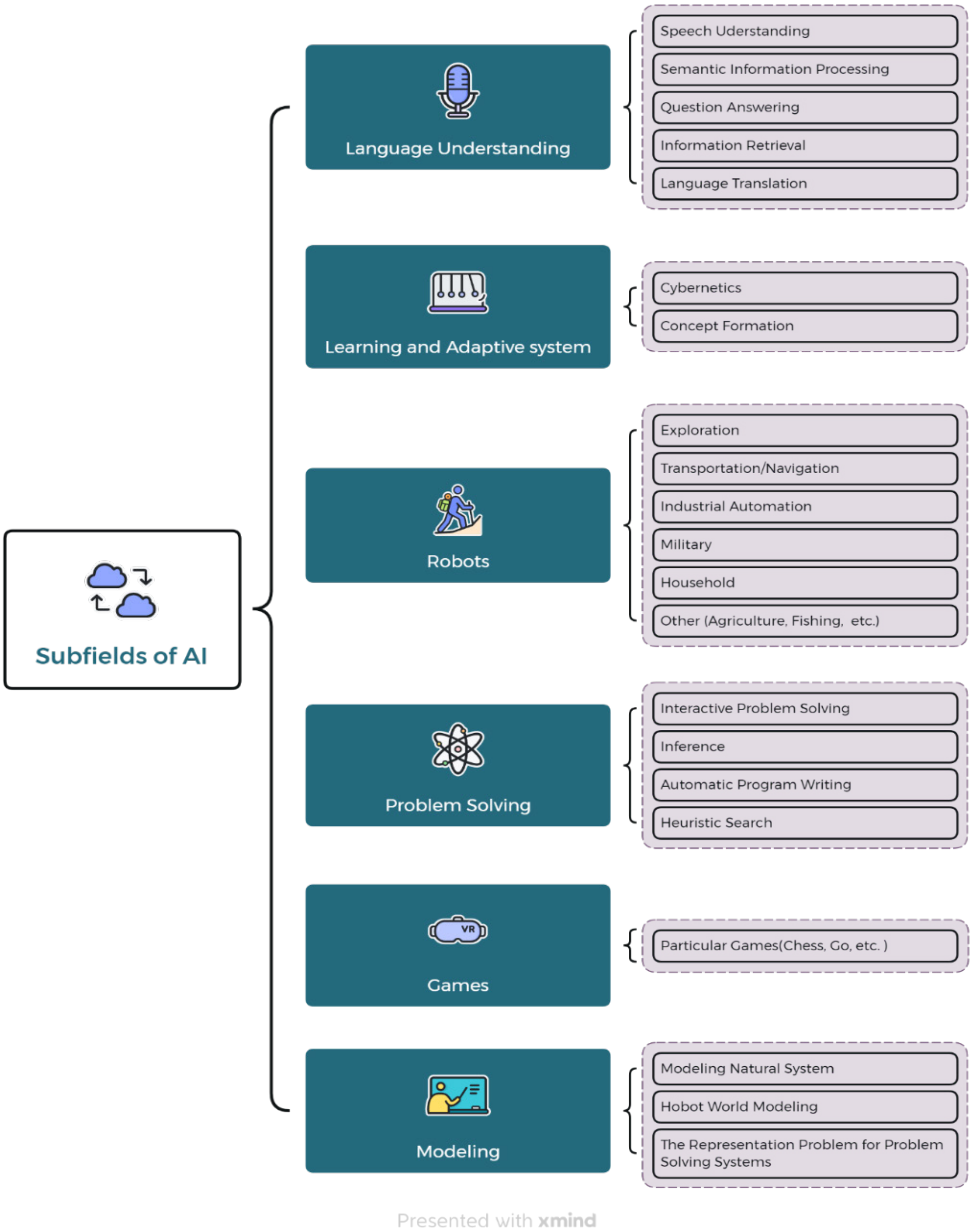

Figure 1. Subfields of AI. AI, artificial intelligence.

esthetic process. In alignment with the Perioperative Surgical Home objectives set forth by the American Society of Anesthesiologists (ASA), optimized perioperative pain control is shown to enhance patient recovery while also conferring societal and economic benefits [14]. However, conventional methods often struggle to achieve optimal pain management outcomes. Inadequate pain control can precipitate a myriad of issues for patients, encompassing both physical and mental health challenges. These may include increased susceptibility to morbidity across various organ systems, the development of depression and anxiety, prolonged pain hypersensitivity potentially progressing to chronic pain, the use of opioids and its associated adverse effects, elevated medical expenses, and a diminution in life quality [13-15].

Overcoming these obstacles and refining perioperative pain management are paramount to bolstering patient recovery and optimizing healthcare provision. In response to the potential issues outlined, medical professionals such as surgeons and anesthesiologists have endeavored to implement improvements. Over the past few decades, there has been a significant evolution in the conceptual frameworks and methodologies underpinning perioperative pain management [16, 17]. The ASA-hosted Pain

Table 1. Summary of works on "Pain Assessment"

Author/Year	Data Type	Patients/ Datasets	Target	Results	Model(best)
2015, Sikka [28]	Videos	50	Pain detection, pain intensity classification	AUC = 0.84-0.94	CVML
2022, Fontaine [29]	Images	2,180 facial expressions	Pain intensity classification (pain intensity>4/10 and >7/10)	ACC = 53% Sensitivity = 89.7%, 77.5%	ResNet-18 CNN
2022, Chen [30]	Images, videos	UNBC-Mc-Master Dataset, Wilkie's Vid-eo Dataset	Pain intensity classification	ACC = 87% AUC = 0.94	MIL, MCIL
2019, Hu [31]	Functional near-infrared spectroscopy	21	Pain detection and localization	ACC = 80.37%	3-layer NN
2021, Han [32]	EEG	67	Pain intensity classification	ACC = 92.54%	LDA
2015, Gruss [33]	Bio-poten-tials	85	Classification (baseline vs. pain tolerance threshold), (baseline vs. pain thresh-old)	Identification rate = 90.94%, 79.29%	SVM
2013, Ben-Israel [34]	Physiological parameters	25	NoL (nociception level) development and valida-tion	AUC = 0.97 R = 0.88	Non-linear Random Forest regression
2021, Gao [35]	Clinical data	300	Pain intensity classification	ACC = 95.6%	BP
2023, Pinzon-Arenas [36]	EDA	36	Pain intensity classification	ACC = 91.5%	1D-CNN, LSTM, CNN-LSTM
2024, Carlini [37]	Facial ex-pression	73	Pain intensity classification	ACC = 77.1% F1 = 80.8% AUC = 76.0%	CNN
2021, Salekin [38]	Visual and vocal signals	Neonatal Pain Dataset	Pain intensity classification	ACC = 79% AUC = 0.87	VGG-Net, LSTM
2021, Choi [39]	PPG	120	Pain intensity classification	ACC = 71.4% AUC = 0.76 Sensitivity = 68.3% Specificity = 73.8%	CNN
2021, Baharloo [40]	Pain intensity measured manually	218	Assess pain's slow/fast dynamics	F score = 0.79 AUC = 0.704	MLP
2016, Nickerson [41]	Clinical data	26,090	Pain intensity classification	MSE = 5.54, 4.96, 5.14, 6.09 Correlation Coefficient = 0.604, 0.606, 0.593, 0.545	Several NN models (Elastic Net)
2015, Tighe [42]	Clinical data	8,071	Pain detection	AUC = 0.643-0.727	Several ML models (LASSO)
2021, Tan [43]	Clinical data	20,716	Pain detection	AUC = 0.763-0.772 Sensitivity = 67.0-69.4% Specificity = 70.9-76.2% PPV = 28.3-31.8% NPV = 93.3-93.5%	Several ML models (Logistic regression)
2023, Llo-rián-Salvador [44]	Radiomics, semantic and clinical features	261	Pain intensity classification	AUROC = 0.62±0.01	ML
2024，Berg [45]	Clinical data	22,707	Pain detection	C statistic (back pain and leg pain) = 0.78(95% CI, 0.77-0.78), 0.76 (95% CI, 0.76-0.77)	ML

Note: If more than one structure/task were investigated in a study, the corresponding information are reported in the same order in which the structures are presented in the "Target"/ "Results"/"Model" columns. ACC, accuracy; AUC, area under curve; CVML, computer vision and machine-learning; MIL, multiple instance learning; MCIL, multiple clustered instance learning; NN, neural network; EEG, electroencephalography; LDA, linear discriminant analysis; SVM, support vector machine; BP, back propagation; EDA, electrodermal activity; PPG, photoplethysmogram; MLP, multilayer perceptron; LSTM, long short term memory; CNN, con-volutional neural network; MSE, Mean Squared Error; PPV, Positive predictive values; NPV, negative predictive values; LASSO, least absolute shrinkage and selection operator; ML, machine learning; Clinical data, it refers to risk factors that may influence patients' cognitive of pain intensity.

Summit in 2019 reached a consensus on foundational principles for the acute management of perioperative pain [18]. These principles include integral preoperative assessment, the adoption of multimodal analgesia, personalized treatment plans, and the necessity for adaptable modifications to care strategies.

Reliable data are derived from clinical registries, administrative databases and so on. Based on the development of AI and the anxious desire for improving the status quo of perioperative pain management in order to follow advanced theories and guidelines, big data analysis has been applied in many fields of perioperative pain management, for example, assessing postoperative pain outcomes, forecasting opioid utilization, evaluating the efficiency of multimodal pain management strategies, and predicting the adverse effect caused by inaccurate pain [19].

In an era marked by the burgeoning individualization, predictability, and complexity in perioperative pain management, AI stands as a powerful tool for navigating and interpreting the intricate tapestry of data relationships. AI's capabilities are particularly well-aligned with the evolving needs of perioperative pain care, which is increasingly reliant on precise, data-driven strategies. This review delves into the synergy between AI and perioperative pain management, examining its integration in the realms of pain assessment, therapeutic interventions, and the prevention of adverse effects associated with suboptimal pain control. At the outset of each section, we provide a concise overview of the field's current landscape. Furthermore, we critically appraise the limitations of this field and speculate on its future trajectory, highlighting the potential of AI to revolutionize perioperative pain care.

AI in perioperative pain assessment

Up to now, most forms of pain assessing instruments applied in the clinical are rating scales, checklists or questionnaires, psychological screening or observational (behavioral) measures. For example, visual analogue scale, verbal rating scale, numerical rating scale and face pain scale are the most frequent tools used for pain assessment, which rely on patients' own appraisal of pain sensory [20-22]. Current methods to measure pain in the clinic are almost restricted to these classical but unidimensional tools while evidence shows there exists some bias. These unidimensional tools cannot always reflect the real reception of pain due to their subjective attributes [23-25].

In addition, the existing pain assessing tools have trouble with infants, critical patients or narcose patients who are unable to speak up, and patients with intellectual disability or dementia who cannot express themselves clearly. Apart from that, inconsistency, slowness and discontinuation of pain prediction are problems to be solved, too.

The use of AI in perioperative pain assessment

Only there is an accurate outcome for pain assessment, can doctors carry out better schemes and adjust plans of drug administration or technique implementation timely for an optimum analgesia [26]. Advantages of AI can help achieve this goal. There has already been a concept called automated pain recognition (APR). APR is an external observation method into which hardware and software components with AI are integrated. Through data collected from diverse parts of human body shown in **Figure 2**, such as facial expression, vocal information, body language, physiological data and so forth, APR can detect, locate, and classify pain [27]. As for the perioperative pain with AI, we divide the current research directions into three parts: facial expression, neural system signals and biopotential and multidimensional factors, combined with AI respectively to measure pain. In this review, 14 papers were identified to be combinations of AI and perioperative pain assessment, and their main features are presented in the **Table 1**.

Facial expression

To explore the secrets between facial expression and pain intensity, researchers have made great efforts, including animal research [46]. Even with high precision in animal experiments, algorithms for human have a long way to go since the quantity of human's facial muscles is too large to locate and analyze. In 2015, Sikka and team introduced a method for evaluating postoperative pain in children using computer vision and machine learning [28]. Their model, trained on facial expressions from 50 patients aged 5 to 18 after laparoscopic appendectomy, showed accurate pain detection and quantification with an area under the curve (AUC) of 0.84 to 0.94. While slightly outperforming nurses and matching parents' assessments, the model's accuracy was the highest under static conditions and was limited to pediatric use. Subsequent research has expanded the use of AI in pain assessment, contributing to a growing body of evidence in this field [28]. Fontaine and colleagues developed a convolutional

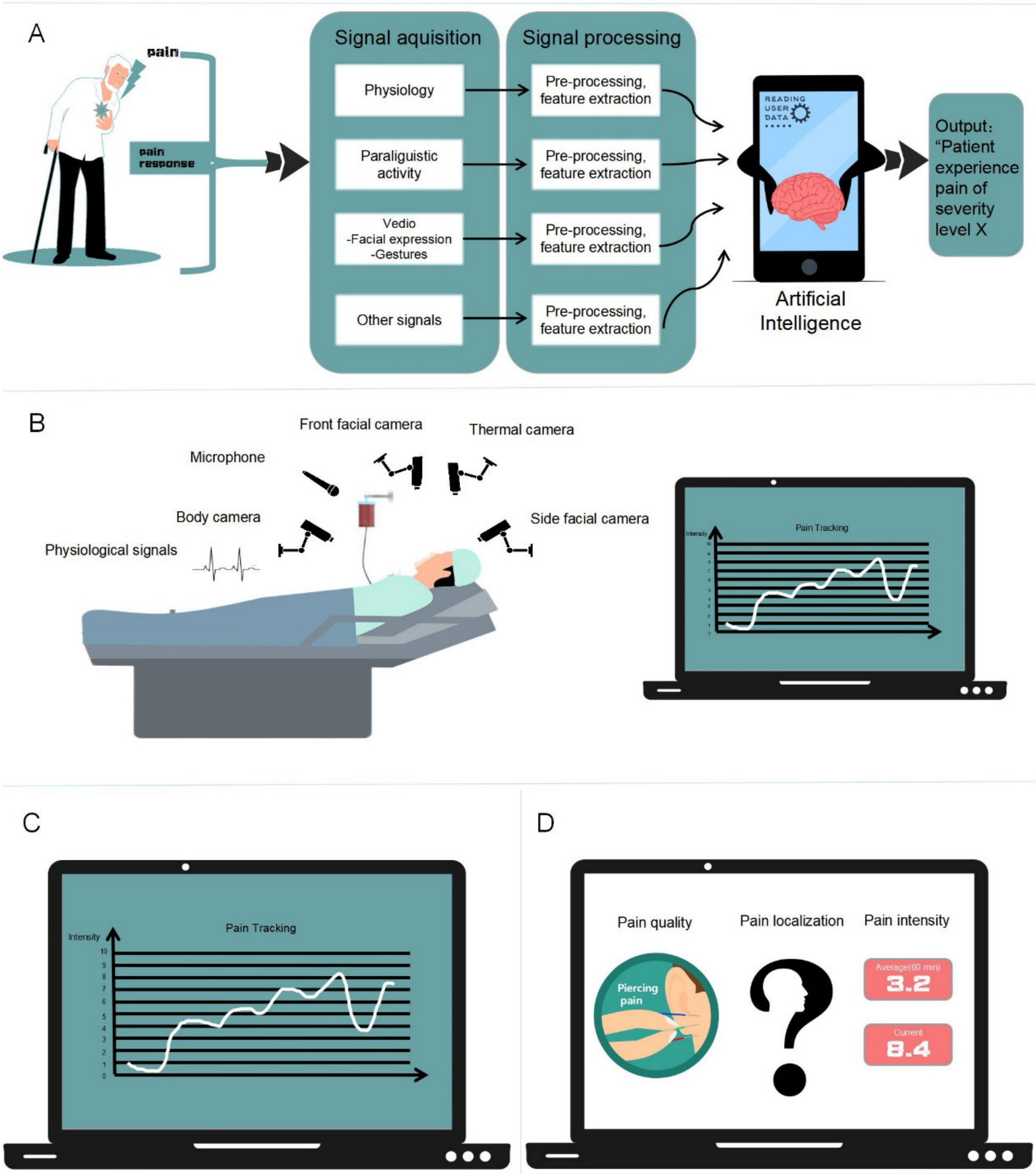

Figure 2. Basis and objectives of automated pain recognition. (A) Data processing in automated pain recognition; (B) Technical infrastructure of multimodality; (C) Monitoring of pain intensity; (D) Proposed monitoring of pain intensity, pain localization and quality.

neural network to analyze facial expressions from 1,189 patients, including 2,810 pre- and postoperative images, to assess pain intensity using the numeric rating scale. The model's performance exceeded that of nurses, with higher sensitivity in detecting moderate (> 4/10) and severe (> 7/10) pain, at 89.7% and 77.5%, respectively, compared to 44.9% and 17.0% in nurses.

However, the overall accuracy of AI (53%) and nurses (14.9%) highlight areas for technological advancement in pain assessment [29]. Chen and team in China created novel data structures to encode facial muscle action units from individual video frames and sequences [30]. Their model achieved 87% precision and an AUC of 0.94 in pain recognition, validated against the UNBC-McMaster Shoulder Pain Expression dataset [30]. In a meticulous analysis, Carlini and collaborators have isolated facial expression features unique to newborns to construct VGG-face and N-CNN deep learning models for the assessment of pain. The study records an accuracy of 77.1%, an F1 score of 80.8%, and an AUC of 76.0% [37]. Pain perception is a profoundly personal affair, and individuals often exhibit alterations in their facial expressions when experiencing intense discomfort. Consequently, the discerning observation of these nuanced changes in expression can serve as a clever means to gauge an individual's state of distress. This approach is particularly beneficial when assessing neonates who are unable to articulate their own feelings, yet its utility among adults with intact language capabilities is comparatively limited.

Neural system signals and biopotentials

As deep researches carried out, certain brain areas have been scoped to be relevant to pain location, severity, duration, and other characters [47]. More and more researchers cast their attention on neural system signals and biopotentials to measure pain. Different stimuli elicit different pain responses, and they are detected by neural imaging instruments combined with given experimental variable as input. For example, on the basis of multivariate pattern analysis, functional magnetic resonance image was used to detect if there are special signals in certain brain areas while positron emission tomography and arterial spin labeling were applied to examine the cerebral blood flow to infer the presence of pain [48]. Electroencephalography derived from cortical activity is a commonly electronical approach to detect pain. In 2019, Hu et al. measured patients' cortical activity during acute pain and used neural network-based AI algorithm to analyze pain diction and location [31]. The data were collected and transmitted into visual images by Augmented Reality devices, in which they achieved an accuracy of 80.37% for pain or no pain discrimination. Neural oscillations combined with AI to predict pain also gained a high precision of 92.54%. Restrained by the limited sample, this study didn't testify the specificality of electroencephalography oscillations to acute pain which may limit clinical localization diagnostics [32]. Beyond neural activity, various biopotentials such as electromyography, skin conductance, and electrocardiography are employed to train algorithms that gauge pain intensity, tolerance, and onset. Our research yielded a 90.94% classification accuracy for distinguishing baseline from pain tolerance, and a 79.29% accuracy for differentiating baseline from pain onset [33]. A predictive model leveraging electrodermal activity as a biomarker for pain has been refined, demonstrating superior performance in detecting severe pain with a precision of 91.5%. Additionally, the model has pioneered continuous pain detection, representing substantial advancement [36].

Other factors

Pain assessment has traditionally relied on unidimensional tools, which are inadequate due to the multifaceted nature of pain [23]. Advances in multidimensional assessments incorporating AI, such as machine learning techniques, have emerged to improve accuracy. Machine learning algorithms have been engineered to analyze data from various parameters, such as plethysmograph waveforms and heart rate, in pre-operative patients, significantly improving the assessment of nociceptive responses. This is evidenced by an AUC of 0.97, markedly superior to the AUCs of individual parameters, which ranged from 0.56 to 0.74. Nonetheless, this method is currently applicable only to patients with ASA physical statuses I-II [34]. In addition, to predict postoperative pain after root canal treatment, Gao et al. collected data from 300 patients undergoing root canal treatment [35]. They established relationships between postoperative pain and 13 biophysical parameters (personal, inflammatory reaction, operative procedure factors) via building neural network models using MATLAB 7.0 neural network toolbox and obtained an accuracy of 95.60%.

Furthermore, data of the pain intensity on early postoperative days, multimodal spatial-temporal approach including signals of vision and hearing, manually measured pain intensity ratings and photolethysmogram spectrograms were exploited to be indicators applied in assessing pain intensity with AUC = 0.87, 0.76, 0.74, respectively. In conclusion, such indicators and algorithms still show space for improvement. As the data mentioned aforesaid in this paragraph, though AUC of machine learning model has achieved 0.97, its application is very limited. So future work may concentrate on indicators which are more easily to capture and analyze. Also, optimizing algorithm for pain prediction or even specified location is deserving expectation [38-40]. Utilizing data from a cohort of 261 volunteers, including radiomics, semantic, and clinical features, researchers have developed a machine learning model capable of predicting the pain response in patients suffering from painful spinal bone metastases. Specifically, the model predicts the comprehensive pain response following palliative radiotherapy [44].

Research indicates that while methods to assess pain generally exhibit good accuracy, those utilizing neural signals and biopotentials as biomarkers achieve higher averages of precision or sensitivity. However, the cost associated with these methods can limit their widespread patient adoption. In response, researchers have focused on enhancing systems by refining algorithms. For example, in a recent prospective multicenter study, a machine learning model was developed to predict postoperative pain following lumbar disc herniation surgery, involving a total of 22,707 participants. The model yielded C statistics ranging from 0.75 to 0.80 for back pain and 0.74 to 0.77 for leg pain predictions [45]. Nickerson et al. built 4 models to evaluate accuracy of pain intensity and found that the Elastic Net performed the best to predict pain intensity with mean squared error of 4.96 and correlation coefficient of 0.606 [41].

Besides, Tighe et al. developed five models to assess their efficacy in predicting severe postoperative pain, with the least absolute shrinkage and selection operator model emerging as the most effective, boasting an AUC of 0.704 [42]. When comparing regression methods to machine learning models for predicting breakthrough pain during labor neuraxial analgesia, the machine learning models edged out the competition slightly. In practical terms, the two approaches exhibited similar performance, with AUCs ranging from 0.763 to 0.772, sensitivities from 67.0 to 69.4%, specificities from 70.9 to 76.2%, positive predictive values from 28.3 to 31.8%, and negative predictive values from 93.3 to 93.5%. These results suggest that further research and algorithmic refinement are necessary to enhance current prediction capabilities [43].

Moreover, each independent study has introduced distinct algorithms for comparative analysis, utilizing a heterogeneous array of data. Consequently, the optimal results from these disparate investigations offer limited utility for cross-comparison. As efforts to refine accuracy persist, relentless exploration remains an imperative. Clinical data, such as vital signs, are relatively accessible, making it objectively informative to learn from these vital signs to predict pain. However, the majority of current studies are retrospective, thereby suffering from a considerable degree of lag.

AI in perioperative pain treatment

In terms of perioperative analgesia, patients hold high expectations on comfortableness, and the requirements of analgesia vary among different patients [49]. To meet patient needs, opioid drug was prescribed beyond their real needs, leading to opioid epidemic, which induced thousands of citizens' addiction and death [50, 51]. Consequently, more flexible and secure techniques are in urgent needs due to the contradiction between patients' ever-growing expectation for better pain management and inadequate antalgic development. To solve this problem, scientists have made unremitting efforts. Thus, patient-controlled analgesia (PCA), a medical device applied in analgesia, which is used for patients to adjust dosage of drugs according to the sensory of pain based on the prescription, was invented [52]. With the development of technology, there are a few types of PCA, from traditional PCA, wireless PCA to AI-assisted PCA which is discussed in this article [53].

Although PCA is one of the most popular technologies applied in analgesia, anesthesiologists also use nerve block in intraoperative general anesthetic or postoperative analgesia courses [14]. Nerve block owns its unique advantages in perioperative pain management, such as a decrease in the opioid use, shortening the length of stay, and a more agreement with enhanced recovery after surgery protocols [16]. However, some problems in the nerve block field remain to be solved. For example, it's hard to precisely localize a nerve, or it may damage important anatomical structures near the target nerve like arteries or other nerves [54, 55]. In this review, we identified a total of 8 articles investigated combinations of AI and perioperative pain treatment, and their main characteristics are reported in the **Table 2**.

AI in pain treatment

As mentioned above, when combined with AI, many things change. In the next paragraphs, we'll discuss how AI is applied in PCA and nerve block.

PCA

Back to 2012, on the premise of having learned 280 attributes of 1,099 patients, Hu et al. developed a predictive model for analgesic dosing [56]. They utilized a decision tree-based algorithm to forecast both total and PCA drug requirements based on the initial two-hour consumption. Their model achieved an accuracy of 80.9% for total dosage and 73.1% for PCA dosage predictions. Despite the labor-intensive process of manually collecting data at the time, another study employed a multi-model regression tree (MRT) approach to analyze the profiles of 3,052 IV-PCA patients, aiming to predict analgesic usage. MRT outperformed their proposed algorithms, human expert predictions, and traditional methods like linear regression and F-text, with the lowest root mean square error. The researchers intentioned to enhance the model by integrating expert knowledge into the MRT system, moving towards a model that is both data-driven and knowledge-driven [57]. Research has suggested that the analgesia nociception index correlates with pain medication

Table 2. Summary of works on "Pain Treatment"

Author/Year	Data Type	Patients/ Dataset	Target	Results	Model(best)
2012, Hu [56]	PCA usage	1,099	Strategies of drug infusion (Total Analgesic Consumption and PCA Analgesic Requirement)	ACC = 80.9% ACC = 71.3%	Decision tree-based learning
2018, Hu [57]	Clinical data	3,052	Strategies of drug infusion	The least RMSE (compared with human experts)	MRT
2018, Gonzalez [58]	ANI signal	15	Strategies of drug infusion	ACC = 81%	Several ML models (SVM)
2020, Nair [59]	Clinical data	13,700	Prediction on drug dosage	ACC = 72%	Several ML models (Random Forest)
2011, Tighe [60]	Clinical data	349	Predict needs for nerve block	AUC = 0.7	Several ML models (AD Tree)
2021, Liu [61]	Ultrasound images	100	Assist nerve block	ACC enhancement = 0.5-12.5%	SegNet Model
2022, Yang [62]	Ultrasound images	1,126	Assist nerve block	ACC = 96% Sensitivity = 97.7% Specificity = 84.6%	CNN
2016, Smistad [63]	CT images	48 ultrasound image sequences	Locate anatomic markers	Average DSC = 0.91	Kalman filter

Note: If more than one structure/task were investigated in a study, the corresponding results are reported in the same order in which the structures are presented in the "Target"/"Results"/"Model" columns. PCA, patient controlled analgesia; ACC, accuracy; AUC, area under curve; RMSE, root mean square error; MRT, multimodal regression tree; SVM, support vector machine; ANI, analgesia nociception index; ML, machine learning; CNN, convolutional neural network; CT, computed tomography; AD Tree, alternating decision tree; DSC, dice similarity coefficient; Clinical data, it refers to risk factors that may influence the dosage of drug or the likelihood one needs nerve block.

dosage, potentially enabling the prediction of drug consumption using AI [64]. By employing various machine learning models, investigators explored the relationship between analgesia nociception index and the administration of intravenous remifentanil. Analysis of data from 15 patients undergoing cholecystectomy surgery at specific time points revealed that the support vector machines (SVM) model yielded the highest accuracy of 81%. However, the small sample size limits the generalizability of these findings [58].

In contrast, Nair et al. analyzed pre-operative data from 13,700 adult patients, including patient characteristics, procedures, and other factors that could influence post-operative pain and opioid consumption [59]. These data were split into training and validation sets for model training and testing. The researchers observed outcomes throughout both the pre-operative and post-operative phases and found only a minimal difference in prediction accuracy between the two periods, suggesting that AI algorithms can effectively predict post-operative opioid usage based on pre-operative data. However, as opioid usage increased, accuracy rates declined from 89% to 43%. It is important to note that this study was conducted at a single center and focused solely on outpatients, which may introduce bias into the results.

AI has indeed enhanced the precision of PCA by improving drug infusion accuracy. However, there are limitations to its application. For instance, the role of genetic and psychological factors in the efficacy of analgesic drugs, as reported in some studies, has not been fully integrated into AI models due to a lack of comprehensive research in these areas and the absence of detailed genomic and psychological patient data [65- 68]. Furthermore, the quality of the data sources could be improved; many studies have been confined to single centers or have utilized datasets that are too limited in scope.

Nerve block

As early as 2011, Tighe et al. gathered perioperative data from 349 patients to develop prediction algorithms [60]. Five different algorithms—

BayesNet, multilayer perceptron, SVM, ADTree, and simple logistic regression—were used to forecast the need for femoral nerve block after anterior cruciate ligament surgery. The ADTree algorithm emerged as the most effective, with an AUC of 0.7 in cross-validation. However, the complexity of machine learning algorithms and the limited understanding among clinical physicians at the time posed a challenge. The study's limitations include a small sample size and the absence of single-unit predictors. Subsequent reports have shown that AI-assisted ultrasound nerve block outperforms traditional methods in terms of accuracy and reduced operation time. The AI model's accuracy enhancement ranged from 0.5% to 12.5%, suggesting more efficient anesthesia and a reduction in post-operative complications, particularly in scapular fracture surgeries [61]. In the realm of nerve localization, AI has shown remarkable prowess. By utilizing AI algorithms, anatomical markers specific to nerves were learned and translated into sonography guidance, facilitating procedures such as inter-scalene, supraclavicular, and infraclavicular blocks. The AI-assisted system significantly enhanced the accuracy of nerve location for anesthesiologists, achieving a 96% accuracy rate, with 97.7% sensitivity and 84.6% specificity [62]. The integration of ultrasound with AI is marked by the attribute of real-time functionality. A real-time 3D vessel reconstruction algorithm, derived from an extended Kalman filter, was employed to locate, allocate, and reconstruct the 3D model of the femoral artery during ultrasound-guided femoral nerve block procedures. This tracking algorithm demonstrated high precision and rapid processing in identifying the anatomical position of the femoral artery, yielding an average dice similarity coefficient of 0.91 [63].

While AI has significantly streamlined nerve block procedures, particularly by improving precision in nerve location, there is ongoing need for advancements. The challenges in nerve block are not confined to the identification of anatomical markers; there are also discrepancies between ultrasound anatomical recognition and the coordination of the needle and probe. Aspects such as the initial scan location, pressure, tilt, rotation, and angulation of the probe needle remain under the control of practitioners. These areas could represent future directions for AI development to enhance its capabilities in nerve block procedures.

Risk prediction of adverse effects associated with pain management

Many factors and reasons contribute to challenges in the process of perioperative pain management, including anesthesia, patients, and surgeries, which give rise to intraoperative hypotension and bradycardia, postoperative urinary retention (POUR) and so on [69]. Among all these factors, opioid use matters a lot. Although multimodal analgesia has been advocated to optimize effects of analgesia and to reduce opioid side effects, opioid usage still plays an important part in pain management and it can bring many side effects like nausea and vomiting, constipation, respiratory depression and so forth [70, 71]. Since adverse effects caused by nerve block could mainly be avoided through locating precisely, details on which are not introduced here. Common and severe adverse reactions resulted from analgesic medications are mainly discussed in the **Table 3**.

AI in adverse event prediction

Overdose of opioid use

Chronic opioid use, previously encapsulated by the term "opioid extended use," is now further complicated by evidence that surgery can become a risk factor [86]. The critical nature of identifying and forecasting opioid overdose looms large. Investigations, such as those led by Karhade, have tested the application of AI in predicting continued opioid prescriptions post-surgery. These trials focused on preoperative data and biophysical patient characteristics from various surgical procedures. Utilizing a dataset of 5,413 patients with lumbar disc herniation, a study evaluated the efficacy of five machine learning models in predicting continued opioid use. Findings highlighted that 7.7% of patients experienced extended opioid prescription, with the Elastic-net Penalized Logistic Regression model exhibiting the least bias and a commendable calibration rate (c-statistic = 0.81), thus emerging as the most effective among the models tested [72]. Subsequent research by Karhade et al. exploring the postoperative opioid use in patients following total hip arthroplasty and anterior cervical discectomy and fusion corroborated the utility of the Elastic-net Penalized Logistic Regression and Stochastic Gradient Boosting algorithms, with c-statistics of 0.77 and 0.81, respectively [73, 74]. In addition, Klemt et al. developed five machine learning models to analyze clinical data and forecast the risk of prolonged opioid use, achieving high accuracy in predictions (AUC > 80%) [75]. These models not only predicted risk but also identified the relative importance of each risk factor, enabling more objective decision-making than subjective expert judgment. Klemt's work highlighted that a preoperative

Table 3. Summary of works on "Adverse Effects Associated with Pain Management"

Author/Year	Data Type	Patients/Datasets	Target	Results	Model(best)
2019, Karhade [72]	Clinical data	5,413	Predict prolonged opioid use	c-statistic = 0.81	Several ML models (Elastic Net Penalized Logistic)
2019, Karhade [73]	Clinical data	5,507	Predict prolonged opioid use	c-statistic = 0.77	Several ML models (Elastic Net Penalized Logistic)
2019, Karhade [74]	Clinical data	2,737	Predict prolonged opioid use	c-statistic = 0.81	Several ML models (Stochastic Gradient Boosting)
2022, Klemt [75]	Clinical data	8,873	Predict prolonged opioid use	AUC > 80%	Several ML models (ANN)
2006, Peng [76]	Clinical data	1,086	Predict occurrence of PONV	ACC = 83.3% Specificity = 85.0% Sensitivity = 77.9% AUC = 0.814	Several classifiers (ANN)
2012, Bassanezi [77]	Clinical data	198	Predict occurrence of PONV	AUC = 0.72	Fuzzy logic
2014, Gong [78]	Clinical data	195	Predict occurrence of PONV	AUC = 0.761 AUC = 0.900	LR, ANN
2016, Wu [79]	Clinical data	195	Predict occurrence of PONV	AUC = 0.734 AUC = 0.929	LR, SVM
2016, Nickerson [41]	Clinical data	26,090 clinical records	Predict occurrence of POUR	ACC = 66.0%	Several ML models (SVM)
2022, Porche [80]	Clinical data	891	Predict occurrence of POUR	AUC = 0.753 Specificity = 68.2% Sensitivity = 72.9% PPV = 43.4% NPV = 88.2%	Combination of binomial logistic model and MLP
2018, Hatib [81]	Arterial waveform	1,334	Predict occurrence of hypotension (before 15min, 10min, 5min respectively)	AUC = 0.95, 0.95, 0.97 Specificity = 88%, 89%, 92% Sensitivity = 90%, 92%, 97%	LR
2021, Lee [82]	Bio-signal waveforms	3,301	Predict occurrence of hypotension (invasive and non-invasive groups)	AUC = 0.897, 0.762 less MAE than non-AI method	CNN
2020, Solomon [83]	Clinical data	62,182	Predict occurrence of bradycardia (3 phases during the procedure)	AUC = 0.81, 0.87, 0.89 PPV at 95% specificity = 0.30, 0.29, 0.15	GBM
2020, Chou [84]	ABP	83,905 ABP waves	Predict occurrence of bradycardia	Specificity = 99.74 ± 0.07% Sensitivity = 93.12 ± 1.24% ACC = 99.37 ± 0.10% Kappa coefficient = 93.92 ± 0.92%.	Several classifiers (DT)
2019, Jungquist [85]	Electronic monitoring biomedical data	60	Predict occurrence of OIRD	ACC = 80%	SVM

Note: If more than one structure/task were investigated in a study, the corresponding results are reported in the same order in which the structures are presented in the "Target"/"Results"/"Model" columns. ACC, accuracy; AUC, area under curve; ML, machine learning; PONV, postoperative nausea and vomiting; LR, logistic regression; ANN, artificial neural network; SVM, support vector machine, POUR, post-operative urinary retention; PPV, Positive predictive values; NPV, negative predictive values; MLP, multilayer perceptron; CNN, convolutional neural network; GBM, gradient boosting machine; DT, decision tree; OIRD, opined-induced respiratory depression; ABP, arterial blood pressure; MAE, mean absolute error; Clinical data, it refers to risk factors that may contribute to an occurrence of a clinical event.

opioid use duration of more than 90 days was a potent predictor of extended postoperative opioid prescription.

The aforementioned studies, while rich in sample size, are limited by their retrospective design, which lacks diverse experimental classification. Furthermore, the samples were drawn from a tertiary referral center, thus potentially lacking broader population representation.

Nausea and vomiting

Postoperative nausea and vomiting (PONV), as one of the most common complications after surgeries, often leads to patient dissatisfaction. Many well-established and potential risk factors were detected or supposed to cause PONV among which intraoperative and postoperative opioid use plays a significant role [87].

In exploring the intersection of AI and prediction of PONV, researchers initiated studies as early as 2006. They constructed an artificial neural network (ANN) from a dataset of 1,086 patient profiles to predict PONV based on multiple risk factors. Concurrently, four alternative algorithms—Naive Bayesian classifier, logistic regression, Koivuranta score, and simplified Apfel score—were developed for comparative analysis. The ANN demonstrated superior performance, with an accuracy of 83.3%, an AUC of 0.814, a sensitivity of 85.0%, and a specificity of 77.9%, asserting its dominance among the five models tested [76].

In a 2012 study, the Eberhart score was extensively utilized to predict PONV in pediatric patients. However, its efficacy has been questioned by the emergence of fuzzy logic systems, which offer enhanced predictive capabilities by analyzing preoperative risk factors. The findings revealed that the Eberhart score achieved an AUC of 0.62, in contrast to the fuzzy logic model, which attained an AUC of 0.72 [77]. But at that time, it remained unknown how much does every risk factor contributes to the occurrence of PONV. Later, new methods were introduced by Wu and Gong et al. in the prediction work looking for better ways of predicting the PONV during the patient-controlled epidural analgesia [78, 79]. Logistic regression model, ANN, SVM obtained great results, with fairly high accuracy and AUC of 0.734, 0.900, 0.929, respectively. Also, they found female sex is the strongest risk factor in patient-controlled epidural analgesia [78, 79]. Pity is that only small samples were collected and were from single center, so deeper research is needed to validate the outcomes.

Urinary retention

POUR affects 5-70% of patients, prolonging hospital stays and raising the risk of urinary tract infections. Anesthesia and analgesic use are key factors contributing to POUR development [88].

In 2016, on the basis of stacked neural network, Nickerson et al. updated the classification neural network, by setting an upper limit on neuron weight vector norms and rectifying linear unit activation functions [41]. They used an updated algorithm to estimate the risk of complications of POUR and obtained an accuracy of 66.0% using classifiers to predict risks of POUR, achieving more powerful results than traditional methods. However, the algorithm could not determine the exact time of POUR onset. Porche et al. developed a model combining a binomial logistic model and a multilayer perceptron, trained on preoperative data including pain and opioid use, to predict POUR incidence [80]. While achieving an AUC of 0.753, the model's specificity and sensitivity for prediction were only 68.2% and 72.9%, respectively.

Hypotension and bradycardia

When conducting epidural analgesia, hypotension is a very common side effect due to physiological principles of this technique, whose incidence ranks from 0 to 50% [89]. There is an even higher incidence of hypotension of spinal-epidural analgesia than epidural analgesia [90]. Intraoperative blood pressure changes in an imperceptible way, so identifying it early helps predict hypotension which may lead to unfavorable patient outcomes like malignant bradycardia, issue hypoperfusion, and organ dysfunction [91].

In 2018, Hatib et al. utilized invasive arterial waveforms to create algorithms capable of predicting intraoperative hypotension with high accuracy [81]. The algorithm accurately predicted hypotension 15, 10, and 5 minutes before it occurred, achieving AUC values of 0.95, 0.95, and 0.97, respectively, with specificities of 88%, 89%, and 92%, and sensitivities of 90%, 92%, and 97%. The precision of the predictions increased as the time of occurrence approached [81]. But it's an invasive approach. If it's non-invasive, it will be more acceptable for it takes safety into account. In 2021, Lee et al. developed algorithms capable of predicting real-time intraoperative hypotension from multiple bio-signals, including arterial pressure waveforms, capnography, photoplethysmography, and electrocardiography [82]. The study compared invasive and noninvasive methods, revealing that multichannel models outperformed single bio-signal models in terms of accuracy and mean absolute error, with AUC values of 0.897 and 0.762, respectively. Nonetheless, the extent of blood pressure decrease and the timing of appropriate medical interventions remain uncertain.

Bradycardia may happen during the epidural or spinal analgesia, and it can also be a subsequence of hypotension [92]. Solomon et al. constructed logistic regression models using preoperative and real-time intraoperative data to predict the occurrence of severe bradycardia following hypotension at various stages of surgery, achieving AUC values of 0.81, 0.87, and 0.89 for induction (TP1), procedure start (TP2), and 30 minutes post-procedure (TP3), respectively [83]. They identified the most significant risk factors for each surgical phase and confirmed the effectiveness of their models. However, by raising the threshold for vital signs, the true incidence of toxic events may be higher than reported. In another research, Chou et al. used arterial blood pressure waves to develop a neural network and decision tree to detect changes predictive of extreme bradycardia, finding the decision tree model to be the most accurate with 99% specificity and accuracy, and a sensitivity of 93.12% [84].

Respiratory depression

Despite the fact that opioid-induced respiratory depression (OIRD) is rare, aftermath of it can be severe, even fatal [93]. Jungquist et al. enrolled 60 patients who underwent surgery, monitoring their respiratory parameters like SpO_2 and end-tidal CO_2 levels on the first day of their surgery [85]. Further, they constructed machine learning models to analyze these data to predict OIRD. With an 80% accuracy rate, their models can predict an OIRD before a real event happens. But this is observational research, lacking higher level of evidence.

Limitations of the current AI techniques

Nowadays, human is at a stage called artificial narrow intelligence, which allows the completion of single task but with narrow border application. Away from superintelligence, there is still a long distance to trek [94].

Firstly, there is significant scope for enhancing the predictive accuracy of AI. Present-day AI systems lack foolproof precision, and even the most rudimentary algorithms can exhibit biases. This is particularly pertinent in the field of medicine, and particularly in anesthesia, where all interventions involve the human body, leaving little room for errors. In the context of pain assessment, as previously mentioned, studies have seldom reported accuracy rates exceeding 90%. Furthermore, the data utilized as input for AI are, at best, historical; this implies that AI learning may be compromised by flawed clinical judgments or the exclusion of certain scenarios [19].

Second, on most occasions, AI technology could only calculate an outcome but is not able to trace the root cause. It seems that what AI probed is the surface of a huge iceberg, but the rest of it hides under the sea level. The practice of anesthesiology needs not only the high sense of accuracy but also detailed analysis of problems detected during surgeries, including the original etiological factors, the whole process of pathophysiology, and at last, the optimum solutions to the problem. It may exist a circumstance that the machine obtains a certain outcome through the database constructed by the clinical data all over the world, but it's hard for the clinicians to determine whether the outcome is true or false according to his or her own clinical experience, let alone to analyze the etiological factors [7]. As discussed above, AI can predict hypotension and PONV, but it remains confusing whether clinicians should carry out measures to change the situation when the alarm is on.

Additionally, systematical and united databases are waited to construct, while this contradicts personal privacy protection to some extent, which presents a large challenge in linking big biomedical data [95]. In the realm of AI applications, a pressing concern has been the ethical dilemmas previously identified in extant research. These encompass a spectrum of principles, including prudence, equity, privacy, responsibility, democratic participation, and solidarity [96]. For instance, AI algorithms exhibit formidable prowess in language and graphical processing, facilitating significant advancements in clinical robotics capable of interacting with patients. Nonetheless, trust remains a paramount issue, encroaching upon the patient-provider relationship and the interface between patients and AI systems [97]. Another case in point is the globally captivating AI chatbot, ChatGPT, which generates convincingly coherent sentences by mimicking linguistic statistical patterns gleaned from vast text databases culled from the internet. However, this convenience has been disruptive to various domains, including academia, prompting numerous publishers to withhold recognition of AI-generated manuscript editing. The implications of such developments are far-reaching and demand rigorous contemplation and regulatory oversight to navigate the complex ethical landscape of AI deployment [98].

Conclusions

In summary, although current AI technologies have their limitations, the potential of AI to tackle complex challenges and to rapidly illuminate complex relationships is evident. This has led to its successful integration into perioperative pain management, enhancing our understanding and paving the way for future developments. This review presents a curated forecast of future research directions in this domain.

Current literature highlights that existing models and algorithms often fall short due to low accuracy and insufficient reliability, usually stemming from single-center or retrospective observational design. Future endeavors may overcome these hurdles by continually refining algorithms to bolster clinical tools for perioperative pain management. As AI and pain management progress swiftly, current research predominantly focuses on integrating AI with mainstream pain management techniques, albeit with limited functionalities. The trend is shifting towards multifaceted pain management strategies to optimize therapeutic outcomes. AI's potential role in the clinic is poised to evolve into a multifunctional entity, possibly encompassing pain assessment, treatment, and prediction of adverse effects in the future.

The future trajectory of each field is discussed, identifying potential opportunities to address current shortcomings. In pain assessment, researchers may identify additional indicators to refine pain intensity measurements, with the advent of next-generation devices expected to offer real-time monitoring during surgeries. Pain treatment may see the development of AI-integrated devices that assist clinicians in drug selection and dosing. AI's role in nerve block procedures could expand to ultrasound guidance, anatomical localization, and precise needle insertion. Predicting adverse effects could be enhanced with future techniques that provide comprehensive analyses and actionable recommendations for practitioners. These envisioned advancements promise to refine the precision and effectiveness of pain management in perioperative care, justifying further research to explore these promising avenues.

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