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Artificial Intelligence and Breast Cancer Management: From Data to the Clinic

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ABSTRACT

Breast cancer (BC) remains a significant threat to women's health worldwide. The oncology field had an exponential growth in the abundance of medical images, clinical information, and genomic data. With its continuous advancement and refinement, artificial intelligence (AI) has demonstrated exceptional capabilities in processing intricate multidimensional BC-related data. AI has proven advantageous in various facets of BC management, encompassing efficient screening and diagnosis, precise prognosis assessment, and personalized treatment planning. However, the implementation of AI into precision medicine and clinical practice presents ongoing challenges that necessitate enhanced regulation, transparency, fairness, and integration of multiple clinical pathways. In this review, we provide a comprehensive overview of the current research related to AI in BC, highlighting its extensive applications throughout the whole BC cycle management and its potential for innovative impact. Furthermore, this article emphasizes the significance of constructing patient-oriented AI algorithms. Additionally, we explore the opportunities and potential research directions within this burgeoning field.

1 | Introduction

Seventy years after its inception, artificial intelligence (AI) is being developed at an unprecedented pace. Predominantly relying on machine learning (ML) and deep learning (DL) methods, AI has demonstrated remarkable superiority in advancing contemporary medicine, particularly, within the oncology field, through continuous innovation [1, 2]. ML encompasses a compilation of intricate algorithms that can effectively handle tasks arising from exponentially growing data by acquiring patterns through iterative processes, resulting in enhanced performance over time [3, 4]. The traditional ML algorithms involve a variety of forms, including random forest, *k*-nearest neighbor, and support vector machine [5]. DL methods fall within the realm of ML and use artificial neural networks composed of multiple layers of simulated neurons, rendering them, particularly, well-suited for image and video processing. The commonly employed DL architectures encompass recurrent neural networks, convolutional neural networks, transformers, and others. DL primarily focuses on

Abbreviations: ADC, antibody-drug conjugate; AI, artificial intelligence; AUC, area under the receiver operating characteristic curve; BC, breast cancer; CAD, computer-aided detection; CDS, clinical decision support; cfDNA, circulating cell-free DNA; ctDNA, circulating tumor DNA; DL, deep learning; LN, lymph node; ML, machine learning; MRI, magnetic resonance imaging; NAC, neoadjuvant chemotherapy; TNBC, triple-negative breast cancer.

acquiring cancer image data-related knowledge by employing convolutional neural networks to learn rules and representations, while iteratively updating the specific parameters to establish accurate and reliable models [1].

AI applications have become widely used for the comprehensive management of all steps of the cancer process, thus establishing new possibilities for cancer research. By leveraging innovative self-supervised learning methods, developing fundamental models capable of encoding intricate medical data has become feasible [6]. The AI field excels in the integration of diverse data models to enable comprehensive tumor screening, diagnosis, drug optimization, and clinical prognostic evaluation through the analysis and assimilation of multidimensional data, including patient clinical information, image data, and molecular characteristics. Furthermore, the capacity for AI to continuously learn from novel data fosters adaptive and iterative enhancements in diagnostic accuracy and treatment effectiveness over time. Although AI clinical applications in oncology are still in the developmental stage with anticipated limited penetration, the continuous integration of AI and medical technology will propel the implementation of technological advancements in precision oncology [2].

Breast cancer (BC) remains a significant global health challenge because of its high incidence and mortality rates [7]. Fortunately, advancements in screening, diagnosis, systematic treatment, and personalized therapy have led to improved survival rates for BC patients [8]. Correspondingly, these patients also face longer treatment and follow-up times, posing challenges for integrated BC management. Additionally, the growing understanding of BC biology and the rapid development of multiomics technologies have comprehensively enhanced patient information with rich imaging data, complete pathological records, deep genomic insights, and more [9]. Given the high prevalence of BC and the need for multivariate data processing and precision treatment approaches, applying AI for early diagnosis, prognostic prediction, and individualized therapy is at the forefront of AI-assisted disease management. These applications have garnered significant attention in clinical practice (Figure 1). However, numerous challenges remain in diagnosing and treating BC, particularly, triple-negative breast cancer (TNBC) and advanced-stage disease, which lack effective treatments and have higher associated mortality rates [10]. Early detection and accurate treatment strategies are crucial for improving patient prognosis and overall quality of life [11]. In the future, further research, enhanced practices, and appropriate regulation will facilitate the broader clinical translation of patient-centered AI to benefit a larger population of BC patients.

Here, we searched the PubMed database (https://pubmed.ncbi.nlm.nih.gov/) for studies published from January 2014 to October 2024 using the terms “breast cancer” and either “deep learning” or “machine learning.” The results suggest that the number of articles related to AI applications in BC has been increasing exponentially over recent years (Figure 2). After carefully reviewing a list of over 3000 papers from the past 3 years, we narrowed down our selection to more than 1000 by eliminating repetitive or unrelated articles, as well as reviews

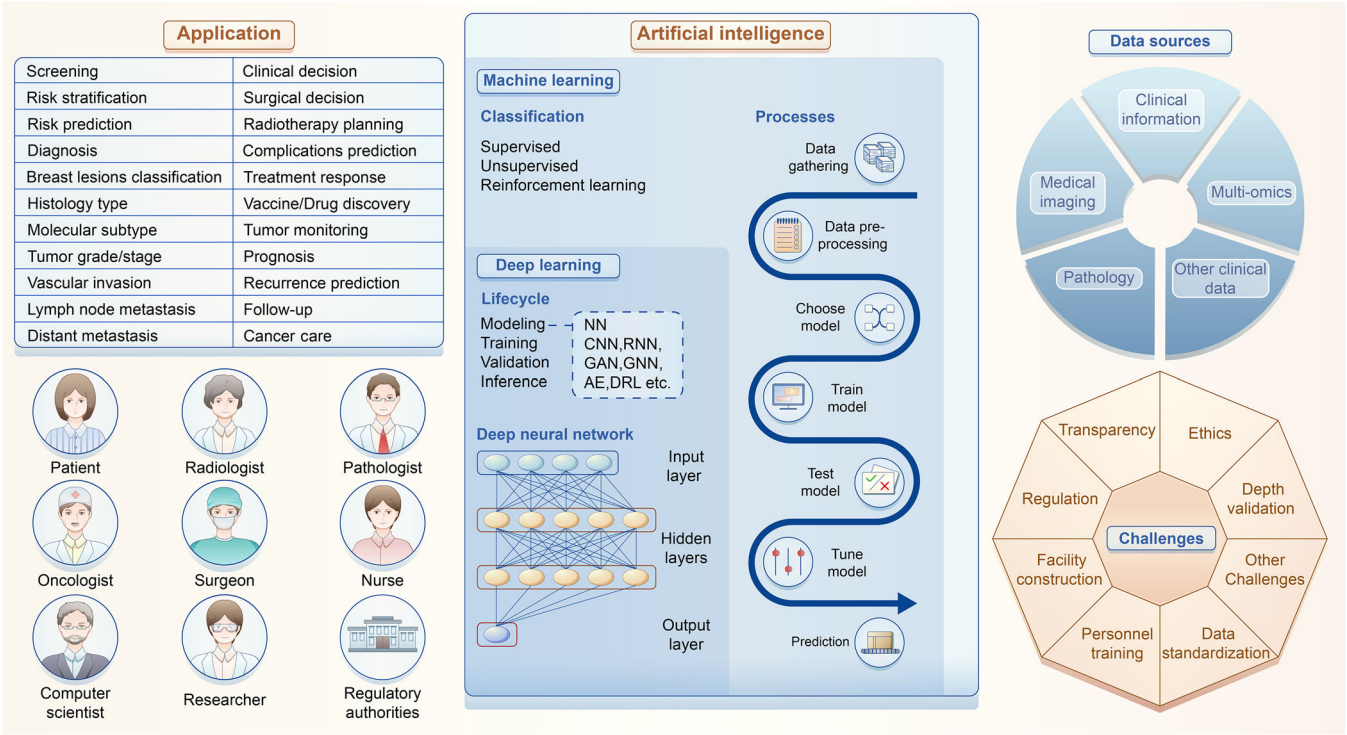

FIGURE 1 | Overview of the whole-cycle involvement of AI in BC management. The application of AI has become prevalent in BC diagnosis, prognosis, and treatment methods. By processing and analyzing clinical information, medical images, and other patient-related data, AI aids healthcare professionals in implementing personalized health management for patients. Furthermore, AI encounters numerous challenges in its clinical applications. AE, autoencoder; AI, artificial intelligence; BC, breast cancer; CNN, convolutional neural network; DRL, deep reinforcement learning; GAN, graph adversarial network; GNN, graph neural network; NN, neural network; RNN, recurrent neural network.

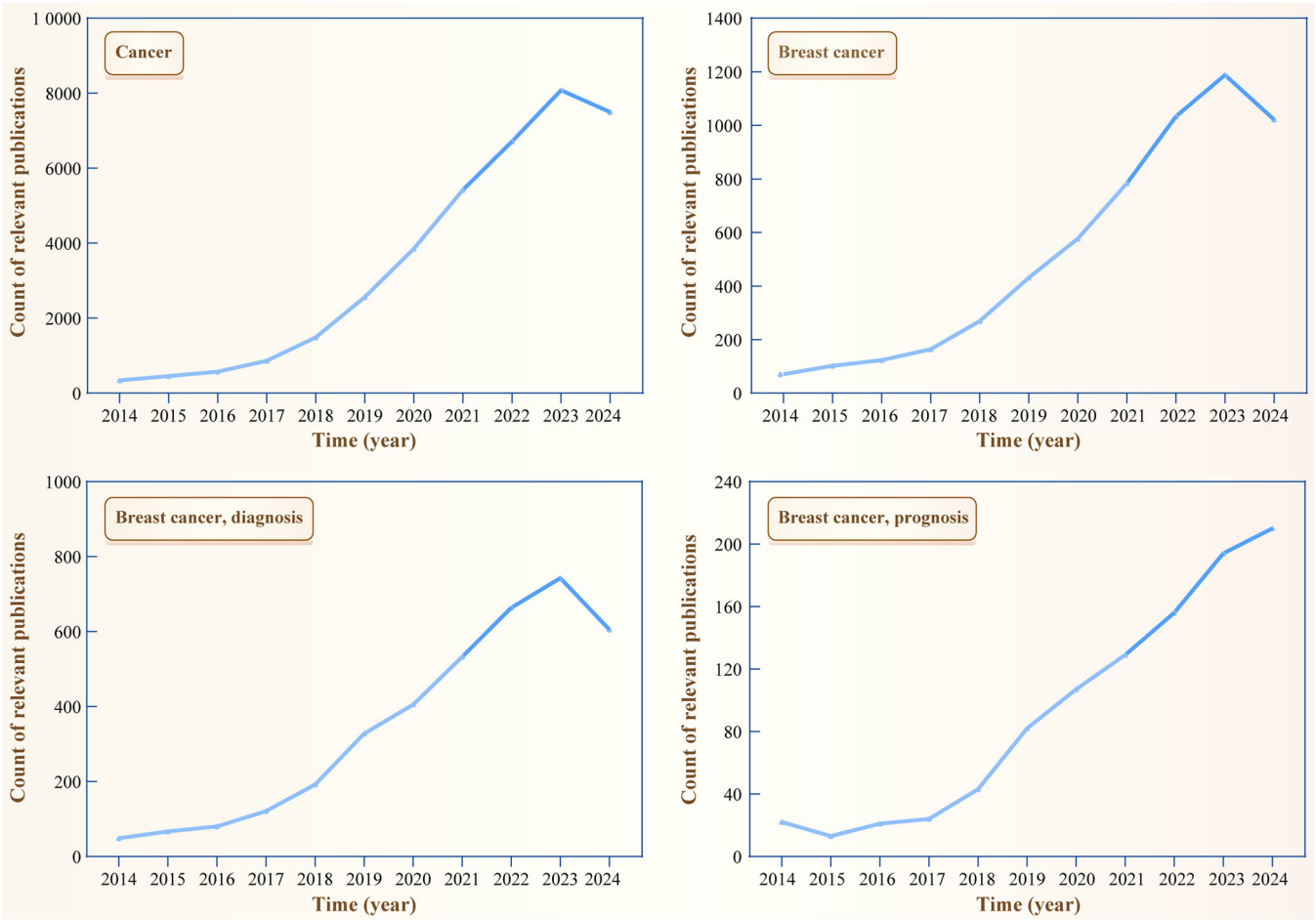

FIGURE 2 | Number of published articles related to the application of AI in cancer and BC, as well as BC diagnosis and prognosis, over the past decade. The PubMed database was searched using the terms "cancer," "breast cancer," "diagnosis," "prognosis," "deep learning," and "machine learning." AI, artificial intelligence; BC, breast cancer.

and systematic reviews. To ensure comprehensive coverage, we included approximately 20 articles under each subheading using factors, such as patient population size, training set size, and test set size.

The objective of this review is to provide a comprehensive overview of the latest advancements and challenges in BC AI applications, as these emerging technologies gradually transition from behind-the-scenes operations to prominent roles, facilitating data translation into clinical applications. This review primarily focuses on the application status and potential of AI in various aspects of BC management, specifically addressing diagnosis, prognosis, and treatment separately. Notably, numerous studies have explored diverse application scenarios rather than focusing on a singular aspect.

2 | BC Diagnosis and Risk Assessment

2.1 | Medical Imaging

There is a long history of computer-assisted improvements in medical imaging performance for BC screening and diagnosis. Computer-aided detection (CAD) was approved in 1998 by the Food and Drug Administration for use in mammography, with widespread adoption following [12, 13]. However, because of limitations, such as false positives and increased recall rates, CAD cannot meet the increased demand for mammography performance [14]. Early detection and diagnosis are key for improving BC patient survival rates. In general, the BC mortality rate has been significantly reduced with mammography-based screening and more effective treatment methods. The 5-year survival rate of early-stage BC is more than 90%. However, the decline in BC mortality has slowed over the past decade [15], likely because the current screening technologies are gradually stabilizing. This suggests that early detection rates are still insufficient, especially for women with dense breast tissue. ML and DL models have showed high accuracy, robustness, and performance for cancer screening and risk prediction in the medical imaging field [2, 16]. DL-based AI algorithms can improve the mammography detection rate and diagnostic accuracy for BC. In a retrospective study, radiologists from multiple institutions found excellent performance when evaluating more than 30,000 pathology-proven cancer-positive mammograms by adding AI. This demonstrates that AI can improve the diagnostic performance of radiologists by overcoming the problems associated with traditional CAD [17]. Another study noted that a system consisting of pretrained black-box predictive AI and learning-delay AI reduced the false positive rate by 25% with the same rate of false negatives, while

reducing the clinician workload by 66%, compared with double-read arbitration in a screening program [18].

In addition to mammography, unique features and rich imaging data, such as ultrasound, magnetic resonance imaging (MRI), and positron emission tomography/computed tomography (PET/CT) scans, can provide opportunities for clinically meaningful AI. The preliminary results of applying AI in these fields have shown advantages [19–21]. Although ultrasound partially compensates for the limitations of mammography, it also faces certain issues, including high false positive and recall rates [22]. Shen et al. showed that an AI system was able to detect cancer with the same sensitivity and higher specificity than radiologists [23]. A hybrid diagnostic model combining predictions from both radiologists and this AI system maintains test sensitivity while reducing the false positive rate by 37.3% and required biopsies by 27.8% [23]. Moreover, using ensemble DL models can identify subtle elements on breast lesion images, further improving the performance and read time of ultrasound images [19, 24]. DL can also combine ultrasound and elastography to predict axillary lymph node (LN) metastasis, which may reduce false positive diagnoses and unnecessary biopsies [25].

There is great potential in applying AI-based risk models derived from medical imaging data to analyze unstructured information, which can enable an accurate assessment of BC risk. AI can be leveraged to directly predict a patient's short-term or lifetime probability of developing cancer [26, 27]. Comprehensive risk prediction models are able to identify high-risk women while reducing interventions for low-risk women, with high discrimination [27]. Currently, the major models used for BC risk prediction are Gail, Tyrer-Cuzick, BOADICEA, and BRCAPRO. Among them, the Tyrer–Cuzick model, which integrates personal history and multigenerational family history, can effectively predict cancer risk [28]. According to a study with a 10-year follow-up period, AI-based risk model images for mammography showed that the AI model was superior to the Tyrer–Cuzick model for both short-term and long-term assessments [29]. An image-based DL method demonstrated superior discrimination of individual risk in a 5-year cancer risk prediction study using breast MRI scans. The area under the receiver operating characteristic curve (AUC) values ranged from 0.544 to 0.732, surpassing the AUC range of 0.401–0.585 achieved with the Tyrer–Cuzick model [30]. For carcinoma in situ, AI supports a higher detection rate than standard screening [31]. Of note, a proportion of patients with early or interval BC may later develop advanced or metastatic disease characterized by refractory, aggressive, and poor prognosis. Therefore, early risk assessment and prediction are necessary for these patients. Vachon and colleagues evaluated mammograms captured within a period of 2 years preceding BC onset, with a maximum of 5.5 years. They showed that Transpara AI algorithms combined with breast density can contribute to improved detection and long-term risk prediction for invasive BC [32]. AI algorithms can identify suspicious areas that may develop into advanced BC, providing screening opportunities for people at high risk of cancer to support early intervention or prevention. This is, particularly, important for predicting cancer with poor prognosis. In another study, an AI model was found to be a powerful predictor for BC risk stratification within 3–6 years after a negative mammogram, providing a better strategy for early screening intervals [33].

The rapid advancement of AI in the breast imaging field presents numerous possibilities for addressing the limitations associated with clinical diagnostic accuracy, time to diagnosis, and consistency. However, careful consideration is still required before its widespread implementation in clinical practice. In the future, integrating AI with comprehensive clinical data and multiple radiomics may potentially surpass the constraints of the current analytical methods for BC screening and risk assessment. This will aid in reducing false positive results, effectively detecting interval cancers, and assisting physicians in achieving accurate diagnoses.

2.2 | Pathology

Pathology has long played a central role in tumor diagnosis. As with noninvasive imaging, the integrated development of AI and pathology has had a positive impact [34]. Overall, the introduction of novel pathological techniques, such as whole-slide imaging, has provided more comprehensive and intricate large-scale data sets that encompass breast fine-needle aspiration specimens or tissue specimens [3, 35]. Applying AI-based digital pathology technology can overcome the inherent limitations associated with the subjective nature of pathologists, including variations in data perception and judgment, thereby effectively reducing their workload. A notable example is the significant improvement in detection sensitivity for micrometastatic BC from 83% to 91%, accompanied by a remarkable reduction in the average detection time by pathologists from 116 s to 61 s through the assistance of DL algorithms [36]. The DL field offers precise and efficient tools to assist pathologists with tasks, such as tumor diagnosis, molecular typing, LN metastasis identification, immune infiltration analysis, and prognosis assessment [37]. The quantitative analysis of tissue markers, such as Ki-67 and HER2, plays a crucial role in BC assessment. However, the evaluation of these markers is somewhat subjective. Abele et al. evaluated biopsy specimens from 204 women with invasive BC. The average intraobserver agreement for Ki-67 between manual interpretation and AI-assisted interpretation was 87.6% (95% confidence interval [CI]: 85.0–89.8) [38]. For ER/PR, it was 89.4% (95% CI: 87.6–91.0). Furthermore, the impact of AI assistance on the interobserver reliability was investigated, with Krippendorff's α slightly increasing from 0.69 (95% CI: 0.65–0.73) to 0.72 (95% CI: 0.68–0.76) [38]. Correctly interpreting the HER2 immunohistochemistry staining results is crucial for the personalized treatment of patients [39]. It can be challenging to distinguish between HER2 0 and 1+ cases. Wu et al. showed that the accuracy of AI-assisted interpretation increased by 13%, with the AI algorithm improving the overall consistency. In HER2 1+ cases, the accuracy was significantly increased by 21% in the case of heterogeneity [40]. Furthermore, AI can address some of the limitations of the current concomitant diagnostic analysis methods that use genomic or tissue biomarkers. The heterogeneity within tumors allows for different spatial locations to generate different diagnostic and prognostic information. AI-based interrogation tools can help overcome this limitation by analyzing all tumor tissue slides to generate comprehensive, consistent features that represent the entire lesion.

Currently, AI methods are mainly used to analyze two-dimensional (2D) pathology images. In contrast, three-dimensional (3D) pathology techniques can generate high amounts of data from cancer specimens in a nondestructive manner, providing a potential opportunity for AI analysis to provide a high-quality comprehensive presentation of the tissue microstructure over a large region of interest [41]. In molecular oncology diagnostic research, especially in the context of extensive data sets and single-cell sequencing-driven high-throughput genomics, data containing high levels of genetic variation need to be supported by a combination of comprehensive molecular analysis and ML to be processed and interpreted at the genetic and clinical levels. This must also be done within a reasonable time frame to assist in clinical decision-making [42, 43]. In addition, analysis of other omics data containing complex and important information, such as proteomics and methylome data, will be inseparable from AI use in the future.

2.3 | Liquid Biopsy

In recent years, using liquid biopsy of body fluid samples, which encompass a diverse range of tumor derivatives, has gained significant traction for BC management. Circulating cell-free DNA (cfDNA), circulating tumor DNA (ctDNA), and circulating tumor cells in peripheral blood have become promising biomarkers for the early diagnosis and dynamic monitoring of disease response and prognosis [44]. One study assessed the use of cfDNA methylation profiling for identifying tumor components and detecting potential tumors with a semireference deconvolution algorithm leveraging tumor scores and ML models, which achieved 86.1% sensitivity and 94.7% specificity for early cancer detection [45]. Methylation sequencing has the potential to improve current cfDNA testing methods. Indeed, abnormal methylation of CpG islands is often widespread during cancer initiation, reflecting early tumor changes. The methylation pattern of cfDNA is consistent with the cell or tissue of origin, but the blood concentration is usually very low. Although the current detection and analysis methods have broad clinical application prospects, there are still many challenges and difficulties, such as the screening specificity and sensitivity [46]. However, using AI-assisted methylation sequencing offers distinct advantages from its ability to detect low-abundance ctDNA information at dilution factors as low as 1/10,000, as demonstrated by Liang et al. [47]. Furthermore, cancer patients often exhibit unique cfDNA fragmentary patterns, and traditional clinical fragmentary studies have focused on genome-wide fragmentation patterns using whole-genome sequencing methods. A recent study used an ML model of the fragmentary patterns of a targeted cfDNA sequencing panel to distinguish multiple cancer types, including BC, and to discriminate cancer from noncancer at very low ctDNA fractions [48]. Predictably, incorporating the cfDNA sequence, methylation status, and fragmentation patterns into the classifier can potentially augment ML cancer detection models, enhance classifier performance, elevate the diagnostic and predictive capabilities of liquid biopsy, and facilitate real-time monitoring of a cancer patient's health status.

Accurate and timely diagnosis and risk prediction are imperative for efficacious treatment and prolonged survival of individuals with BC, representing persistent challenges in the field [49]. The potential of AI for clinical applications, such as imaging, histopathology, and liquid biopsy, is noteworthy. Nevertheless, applying AI often faces issues, such as overfitting and model generalization. The successful clinical translation of AI and provision of optimal patient service necessitate large-scale, multicenter, high-quality prospective studies to sufficiently validate AI models. Moreover, enhanced transparency, improved interpretation, and appropriate regulation are all required.

3 | BC Prognosis Prediction

BC patient prognosis is influenced by a multitude of intricate factors, including age, family history, lifestyle, and pathological characteristics. Promptly predicting cancer prognosis poses a multifaceted challenge [50]. By integrating various data sources to construct survival prediction models, AI can assist clinicians with more accurately forecasting patient outcomes. A study conducted by Xiao et al. revealed that the random survival forest model exhibited a slightly significant improvement over the traditional Cox regression model for discrimination power, which was potentially attributed to its enhanced capability of detecting and elucidating higher-order interactions, as well as nonlinear relationships [51]. Random forest is a commonly used model for BC survival prediction, as it is easy to adjust and interpret and can handle high-dimensional nonlinear features with high generalization [52, 53]. In addition, the ML algorithm XGBoost model has demonstrated significant clinical utility for predicting the prognosis of BC patients with brain metastases. This model exhibited excellent performance in external independent data sets, with a survival AUC value exceeding 0.8 from 6 months to 3 years [54]. Of note, the widespread application of these models remains to be carefully considered. A recent large cohort study in the United Kingdom reported that statistical regression models performed similarly to or better than ML models in predicting the 10-year risk of BC-related death among women at any stage. Compared with Cox proportional hazards and competing-risk regression methods, XGBoost or neural networks showed complex miscalibration patterns and unstable calibration of cancer stage groups [55]. Although the study did not adequately incorporate other data sources that could potentially enhance its predictive capabilities, its results still suggest that certain limitations of the ML predictive model necessitate further refinement for enhanced clinical utility. This also underscores the need for cautious implementation of open-bag AI and acknowledges its current inability to fully supplant traditional prognostic prediction methods. Early prediction of recurrence in BC patients is helpful for developing personalized treatment plans and post-operative follow-up strategies, as well as for improving survival rates [52]. TNBC patients are more likely to experience metastatic recurrence and death than patients with other BC subtypes [52, 56]. An advanced DL-based image analysis model has enabled the objective and highly reproducible assessment of tumor-infiltrating lymphocytes. A multiscale embedded DL framework can capture and quantify cancer-related LN changes that are not limited to the presence and size of cancer cell deposits. Furthermore, using ML workflows to assess tertiary lymphoid structure and tumor budding, as well as the comprehensive analysis of their correlation, holds significant value

in prognosticating recurrence and evaluating TNBC patient prognosis. These methods hold significant value in predicting recurrence and evaluating prognosis for these individuals [57, 58].

Exploring potential survival predictors through large-scale data analysis is also an important reflection of the involvement of AI in personalized prognosis prediction [59]. Traditional pathological factors, such as tumor type, LN metastasis status, and serological indices, are insufficient to meet the needs of personalized treatment. Multiomics, including genomics, has played an important role in the development of BC biomarkers [60]. However, manually exploring the key genes or gene clusters in a large set of high-dimensional data has remained a challenge. Mirza et al. integrated multiple microarray data sets by employing a variety of ML methods, using disease-free survival and overall survival analyses to identify eight key genetic prognostic biomarkers (CCNE2, NUSAP1, TPX2, S100P, ITM2A, LIFR, TNXA, and ZBTB16) [61]. Zheng et al. combined clinical features and transcriptome analysis with ML screening of prognostic biomarkers and applied the LASSO-Cox regression coefficient to construct a risk model [62]. Prognostic models with more patient information and clinical trials can help achieve better clinical data practicability and more efficient and accurate treatment planning and clinical decision-making.

4 | BC Treatment

4.1 | Drugs

Drug therapy for BC treatment is rapidly evolving, including the use of endocrine inhibitors, targeted therapeutics, immunotherapy, and antibody-drug conjugates (ADCs). Therefore, it is, particularly, important to predict treatment response, explore drug combinations, or discover new drugs to prevent resistance and improve prognosis. Multitasking model suites using integrated genomes, targets, drug structures, bionetwork data, and effect-based characteristics help to personalize drug or combination response prediction and guide treatment selection to maximize efficacy and minimize toxicity [63, 64]. The objective tumor response rate of first-line treatment with CDK4/6 inhibitors is less than 50%, and conducting a comprehensive analysis with the construction of interpretable DL for the tumor gene profile can predict the effectiveness and resistance of palbociclib for BC [65]. Sammut et al. used ML approaches that integrated clinical, molecular, and digital pathology data to predict treatment responses [63]. These models were externally validated and showed excellent discrimination over models that used clinical variables [63].

Neoadjuvant chemotherapy (NAC) has become the established standard of care for BC treatment for tumor size reduction, downstaging, and improved rates of breast conservation surgery. A patient's response to NAC also plays a pivotal role in predicting treatment efficacy and guiding subsequent therapeutic decisions. However, because of inherent tumor heterogeneity, responses to NAC often exhibit significant variability [66]. The early and accurate prediction of treatment response can facilitate timely treatment regimen adjustments, which would benefit patients with poor response to NAC. Multiple DL models have demonstrated superior overall performance in evaluating the effects of NAC compared with some conventional response prediction methods (Table 1). In a retrospective study, one model focused on MRI-based quantitative intratumor heterogeneity measures, combined with clinicopathological variables and conventional radiomics. This model displayed excellent performance in predicting the pathological complete response to NAC (AUC = 0.83–0.87) [72]. Yu et al. integrated DL radiomics and clinicopathological information to construct an outstanding NAC response prediction model, using transfer learning to address overfitting issues in small sample size and imbalanced medical image data set [71].

The drug discovery field is associated with challenges characterized by exorbitant costs, lengthy development cycles, and a low success rate in drug development. Moreover, less than 5% of drugs successfully pass oncology clinical trials to gain approval of the Food and Drug Administration [75]. AI has emerged as an invaluable tool across various stages of the drug discovery pipeline, encompassing novel drug design, analysis of drug reactions and reverse synthesis, and molecular optimization and screening (Figure 3) [76]. By analyzing and interpreting vast amounts of biological, chemical, and clinical data, AI can be trained to accurately identify compound hits and drug molecular structures. It can also rapidly verify drug targets and optimize drug structure designs. A recent study has demonstrated that an AI-based Linear design tool was highly

TABLE 1 | Recent studies that employed AI for predicting BC patient responses to neoadjuvant therapy.

Data sources	Method	Training cohort (*n*)	Testing cohort (*n*)	AUC	Refs.
Ultrasound	Automated and reusable DL	1727	685/144	0.83	[67]
PET/CT	Deep semisupervised transfer learning	1019 (all)		0.76	[68]
Pathology	CNN	926	126	0.88	[69]
MRI	KNN, SVM, and so on	70	70	0.96	[70]
Ultrasound	Four different deep CNNs	420	183	0.94	[71]
MRI	Imaging-based decision tree models	335	1254	0.87	[72]
MRI	Multilayer perception, and so on	409	343/170/340	0.93	[73]
Pathology	Federated learning	449	237	0.78	[74]

Note: The selected AUC refers to the optimal value obtained from the validation set mentioned in the citation. Please refer to the original for the exact value.
Abbreviations: AUC, area under the receiver operating characteristic curve; CNN, convolutional neural network; DL, deep learning; KNN, *k*-nearest neighbor; MRI, magnetic resonance imaging; PET/CT, positron emission tomography/computed tomography; SVM support vector machine.

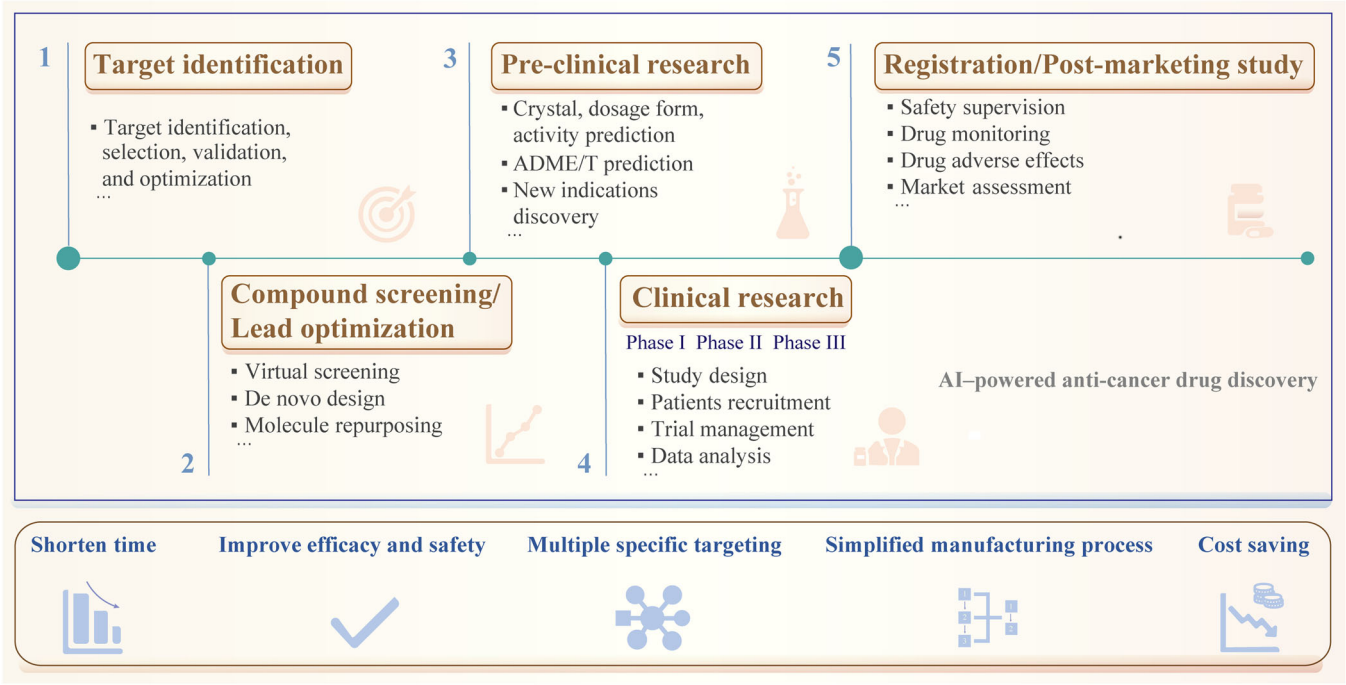

FIGURE 3 | AI-powered anticancer drug discovery. AI applications in the drug discovery pipeline, including target identification, clinical trial development, and registration, offer notable advantages, such as enhanced efficiency and cost savings. ADME/T, absorption, distribution, metabolism, excretion, and toxicity; AI, artificial intelligence.

efficient in vaccine development. The messenger RNA (mRNA) vaccines and drugs generated using this AI tool exhibited exceptional accessibility, optimized stability, and encoded the necessary epitopes. Consequently, they can provide valuable support for further advancements in mRNA-based anticancer drug research [77]. Additionally, the continuous advancement of DL offers enhanced prospects for protein structure prediction and drug design [78, 79]. For example, the AlphaFold tool has successfully elucidated the structures of approximately 200 million proteins, encompassing nearly all known proteins [80, 81]. In recent years, ADCs, which can exert both the cytotoxic effects of small molecule chemotherapy drugs and tumor-targeting effects of antibody-based drugs, have attracted wide attention [82, 83]. Drugs, including trastuzumab emtansine and trastuzumab deruxtecan that target HER2, as well as sacituzumab govitecan that targets TROP2, have demonstrated significant clinical therapeutic efficacy [84–86]. However, these novel and efficient third-generation ADCs also face various challenges, such as complex pharmacokinetic characteristics and toxic side effects [82]. Applying AI in ADC development and innovation is worth exploring further. The use of AI in large-molecule drug discovery is also rapidly increasing. In oncology, large-molecule drugs are expected to account for about 50% of market revenue by 2030, suggesting that AI may establish additional opportunities for developing BC therapeutics [87]. With the advent of the AI-driven drug discovery era, AI-derived drugs are being increasingly implemented in clinical research, which may significantly alter the BC treatment landscape and further improve patient prognosis. The efficient resolution of complex chemical and biological spaces and adverse reactions will continuously improve the overall quality of drug design research and benefit the clinical translation of AI-based drug discovery.

4.2 | Surgery

AI is gradually revolutionizing the surgical field and holds significant value in tumor esthetics, preoperative planning, intraoperative guidance, and postoperative evaluation. The integration of radiomics, pathology, and other data sets has enabled more precise, safe, efficient, and satisfactory surgical decision-making [88]. One study used ML algorithms to predict breast satisfaction during follow-up for women considering mastectomy and reconstruction as part of their BC treatment plan [26], which provided a personalized reference. Furthermore, patterns and associations are employed for anatomical visualization and surgical navigation to assist surgeons in achieving accurate procedures and optimizing postoperative outcomes [89]. ML algorithms also play a crucial role in the timely prediction of postoperative complications or prognosis, such as lymphedema, with improved accuracy and effective anticipation of postoperative pain levels. They can also facilitate the assessment of postoperative risks and mortality rates, allowing for timely interventions to enhance treatment efficacy and optimize postoperative care protocols, while extending survival time [90–92]. AI has broad application prospects in the surgical scene, such as being applied to surgical training to improve the experience of young surgeons and increase their understanding and depth perception [93, 94]. When applied to surgical implant materials, AI-driven 3D printing technology has accelerated the construction of new engineered tissue structures and promoted personalized organ substitutes for patients. 3D/4D printed implants loaded with chemotherapeutic drugs, such as paclitaxel and fluorouracil, have shown high customization ability and good anticancer activity [95, 96]. We infer that in the future, AI models integrating breast shape and size with patient clinical treatment information may produce surgical materials that

better fit the natural shape of the patient's breast and personalize their treatment plan. There is currently a gradual increase in robotic surgery research for BC, especially for breast-conserving surgery and minimally invasive surgery [97]. The integration of ML, machine vision, and haptic control into surgical robots can facilitate human–computer interactions and intelligent task planning and operation [98]. In summary, AI applications in various emerging technologies are reshaping surgical treatment approaches for BC.

4.3 | Radiotherapy

Radiotherapy plays a pivotal role in the standard management of cancer. In the BC clinical setting, AI research has primarily focused on precise image segmentation and treatment planning [99, 100]. Effectively delineating the region of interest and accurately segmenting the clinical target volume are increasingly crucial to align with the evolving trend of precise dose distribution and minimize the risk of locoregional recurrence, as well as side effects. However, various limitations have resulted in a high reliance on clinicians for breast clinical target volume segmentation [99]. DL algorithms for regions, boundaries, dosimetry, and other indicators have been empirically demonstrated to be effective, consistent, and time-saving in the context of automatic segmentation tasks [101, 102]. In general, AI-based automation has emerged as a prevailing trend in BC radiotherapy planning [103]. In the forthcoming years, diverse advanced radiation and delivery technologies, along with multiomics integration, will serve as guiding factors for further advancements in radiotherapy [104]. These factors will pose challenges to the personalized selection of radiotherapy plans encompassing appropriate methods of treatment delivery accuracy and planning efficiency. However, they also present opportunities for leveraging AI capabilities.

4.4 | Immunotherapy

Immunotherapy, particularly, immune checkpoint inhibitor therapy, has displayed promising results for BC treatment. However, the response rates vary among individual patients [105]. The KEYNOTE-355 trial revealed that the combination of pembrolizumab with chemotherapy resulted in longer overall survival compared with chemotherapy alone, especially for patients with a programmed death-ligand 1 (PD-L1) combined positive score of 10 or higher. Notably, within the intention-to-treat population, 40.8% of patients receiving the combination therapy achieved a confirmed objective response [106]. The aforementioned trials provide evidence of the potential efficacy of immunotherapy and justify further investigation. Moreover, it is crucial to promptly assess patient responses to ongoing treatment for clinicians to properly adjust their therapeutic strategies [107]. Digital pathology analysis and AI methods have been used to accurately examine programmed cell death protein 1/PD-L1 expression levels, tumor mutational burden, and tumor microsatellite instability status [108]. An AI-driven approach also further enhanced the potential of predictive biomarker discovery in immuno-oncology [109]. Additionally, AI integrated with high-dimensional data, such as single-cell transcriptomics and spatial transcriptomics, has been employed for predicting the composition and spatial distribution of cells within the tumor microenvironment (Table 2), thereby aiding in antibody design and immunotherapy prediction [64].

4.5 | Clinical Decisions

The increasing availability of therapeutic options and the proliferation of patient clinical imaging methods and pathological information have posed a challenge in selecting the appropriate individualized treatment plan for patients [63]. The proactive identification of patients who are most suitable for a specific treatment can help mitigate the risk of adverse clinical outcomes. In traditional clinical practice, clinicians often use a comprehensive analysis of clinical information, combining their experience, clinical guidelines, and trial guidance, to select and formulate appropriate treatment plans for BC patients. The clinical decision support (CDS) algorithm integrates cutting-edge medical knowledge and calculates the probability of patient outcomes using input digital variables, which encompass the comprehensive medical information of relevant patients. The algorithm integrates cutting-edge medical knowledge and uses input digital variables, namely patient medical information, to calculate the probability of patient outcomes [115], primarily simulating the clinical thinking process. The DL-based CDS that facilitates physician decision-making in an interactive manner between humans and computers can provide reliable evidence-based recommendations and real-time capabilities. This can empower clinicians to make timely and effective treatment decisions for BC, particularly among high-risk patients. Li et al. developed a knowledge graph-based CDS that outperformed clinicians in terms of adherence to first-line therapy [116]. Furthermore, modeling patient trajectories has the potential to enhance CDS [117]. ML algorithm-based CDS methods can facilitate the early identification and implementation of tailored psychological interventions for high-risk women [118]. In addition to supporting clinical decision-making, CDS also plays a pivotal role in the development of smart hospitals, encompassing various aspects of enhancing care quality, such as medication monitoring, medical record quality control, clinical warning alerts, and patient experience surveys [119–122]. CDS is gradually being integrated into clinical practice and expanding its reach to primary healthcare institutions. To effectively adapt to the intricate realities of medical environments, CDS strives to enhance physician autonomy, safeguard privacy, improve transparency, and continuously update itself among other areas that require further refinement. While algorithms cannot entirely replace clinical judgment, their judicious application can help mitigate malpractice risks and further enhance medical services.

There is still a long way to go before AI can guide the full-scale management of BC. The construction of simple and efficient AI models that can be adapted to a variety of scenarios and manage multiple clinical processes is conducive to the promotion of clinical practice, homogenization of medical resources, and efficient management of BC in underdeveloped regions. To better serve patients both pre- and posttreatment, it is also necessary to improve the clinical fit and integrate

TABLE 2 | Recent studies on using AI for BC immunotherapy prediction.

Data sources	AI model	Evaluation focus	Main finding	Refs.
Pathology, genomics, clinical data	ML	Multiple characteristics	The AI-supported model accurately predicts ICI response and survival in multiple tumors based on six characteristics of patients, effectively stratifying patients.	[110]
Pathology	DL	PD-L1	The DL system accurately predicted PD-L1 expression from H&E staining images in a cohort of 3376 patients (AUC = 0.91–0.93), with consistent confirmation from external validation data sets.	[108]
Pathology	DL	PD-L1	The assistance of AI eliminated any notable disparity in PD-L1 CPS interpretation results among pathologists, while also boosting the intra-group correlation coefficient from 0.62 to 0.93, further enhancing result accuracy.	[111]
Pathology	DL	TIL	The TME's immunophenotype can be accurately predicted for different tumor types using a DL model based on TIL analysis, enabling precise determination of the response to ICI treatment.	[112]
Genomics	ML	Macrophage	By integrating scRNA-seq data, the model incorporating macrophages and ML was constructed, demonstrating significant advantages in predicting ICI treatment efficacy and prognosis for patients.	[113]
Radiomics, clinical data	DL	CT, Clinical characteristics	An ML-based imagomics model accurately and robustly measures ICI responses, enabling individualized treatment decisions unaffected by PD-L1 state and other conditions.	[114]

Abbreviations: AUC, area under the receiver operating characteristic curve; CPS, combined positive score; CT, computed tomography; DL, deep learning; H&E, hematoxylin-eosin; ICI, immune checkpoint inhibitor; ML, machine learning; PD-L1, programmed death-ligand 1; scRNA, small conditional RNA; TIL, tumor-infiltrating lymphocyte; TME, tumor microenvironment.

multiple AI models combined with their comprehensive clinical information.

5 | Conclusions

From early diagnosis and risk prediction to treatment plan formulation, treatment response evaluation, vaccine/drug discovery, and prognosis assessment, AI has been extensively employed across all facets of BC management. The deep integration and mutual facilitation of AI and oncology, including BC, have emerged as the future direction of the field. However, numerous challenges and obstacles still hinder its widespread clinical adoption. Further innovations using AI will enhance the efficiency of tumor diagnosis and precision treatment while offering greater possibilities for improving human survival rates and quality of life. To optimize the benefits for BC patients, it is crucial to develop and implement AI technologies in a manner that ensures safety, trustworthiness, and patient-centricity.

Author Contributions

Kaixiang Feng: writing – original draft (lead), writing – review and editing (equal). **Zongbi Yi:** conceptualization (equal), funding acquisition (lead), supervision (equal), writing – review and editing (lead). **Binghe Xu:** conceptualization (equal), funding acquisition (equal), supervision (lead), writing – review and editing (lead).

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Ethics Statement

The authors have nothing to report.

Consent

The authors have nothing to report.

Conflicts of Interest

Professor Binghe Xu is the member of the *Cancer Innovation* Editorial Board. To minimize bias, he was excluded from all editorial decision-making related to the acceptance of this article for publication. The remaining authors declare no conflict of interest.

Data Availability Statement

The authors have nothing to report.

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