Cholangiocarcinoma Evaluation via Imaging and Artificial Intelligence

Chun Mei Yang Jian Shu

Department of Radiology, The Affiliated Hospital of Southwest Medical University, Luzhou, PR China

Keywords

Cholangiocarcinoma · Imaging evaluation · Artificial intelligence

Abstract

Background: Cholangiocarcinoma (CCA) is a relatively rare malignant biliary system tumor, and yet it represents the second most common primary hepatic neoplasm, following hepatocellular carcinoma. Regardless of the type, location, or etiology, the survival prognosis of these tumors remains poor. The only method of cure for CCA is complete surgical resection, but part of patients with complete resection are still subject to local recurrence or distant metastasis. **Summary:** Over the last several decades, our understanding of the molecular biology of CCA has increased tremendously, diagnostic and evaluative techniques have evolved, and novel therapeutic approaches have been established. **Key Messages:** This review provides an overview of preoperative imaging evaluations of CCA. Furthermore, relevant information about artificial intelligence (AI) in medical imaging is discussed, as well as the development of AI in CCA treatment.

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Introduction

Cholangiocarcinoma (CCA) is a malignant neoplasm arising from the biliary epithelium and peribiliary glands [1], representing 10% of hepatobiliary tumors and 2% of malignant tumors [2, 3]. Traditionally, CCA is divided into three types based on anatomic location or growth pattern, including intrahepatic cholangiocarcinoma (ICC), perihilar cholangiocarcinoma, and distal cholangiocarcinoma [4]. The prognosis of CCA is very poor. The current 5-year survival rate after surgery rarely exceeds 35%. Despite the relative rarity of CCA, the incidence and mortality rates of the disease have been reported to be gradually increasing worldwide, and it is the chief cause of nearly 20% of the deaths from hepatobiliary cancers [5, 6]. Epidemiological investigations have indicated that men have a 1.5-fold increased risk of CCA development when compared with women [7].

The only effective way to cure CCA is complete surgical resection, which is only appropriate for patients with well-localized lesions. However, late presentation in many cases results in vascular encasement with lymphatic and perineural invasion, and curative surgical resection

with negative tumor margins can only be offered to less than 30% of patients [8]. Furthermore, 20–50% of patients considered resectable based on preoperative work-up are found to have unresectable disease during exploration [9, 10]. Therefore, it is critical to accurately evaluate CCA for optimal treatment planning and for determining prognosis.

To date, multiple imaging techniques have been utilized for preoperative evaluation of CCA, including ultrasonography (US) [11–13], computerized tomography (CT) [14–16], positron emission tomography (PET) [17, 18], magnetic resonance imaging (MRI) [19–21], and cholangioscopy [22, 23]. Meanwhile, artificial intelligence (AI) techniques have influenced changes across healthcare and have been used in many biomedical areas, especially oncology [24]. Now, the application of AI, allowing machines to better represent and interpret complex data, has been increasing gradually in CCA evaluation [25–28].

Preoperative Imaging Evaluation of CCA

Although the gold standard of diagnosis, grading, and staging for CCA is still pathological examination, it is an invasive method and not appropriate for all patients with CCA. Recent studies indicate that imaging methods can also provide an accurate preoperative evaluation of CCA, resulting in better treatment selection and improved prognosis.

Ultrasonography Technique

Ultrasonography (US) is frequently the initial imaging modality performed to evaluate patients who are suspected to have biliary obstruction or a liver mass, in real time and noninvasively. Early studies on patients with obstructive jaundice praised the ability of US to identify bile duct dilatation and deplored its inability to accurately identify the pathogenesis of biliary obstruction. However, the results of some later studies, which were carried out with modern high-resolution US equipment, have countered these initial impressions. The sensitivity and specificity of US in the detection of perihilar cholangiocarcinoma have risen over the past 15 years, from a reported low of 33% in 1983 to a reported high of 96% in 1996 [29, 30]. It may allow avoiding more invasive procedures in some patients and help identify those patients for whom further investigation combined with modern color Doppler imaging, contrast-enhanced US, and so on might be useful.

Contrast-Enhanced US

Contrast-enhanced US has been reported to be used in preoperative evaluation of CCA – for example, the vascular pattern of the tumor, differential diagnosis with hepatic inflammatory lesions, and correlation with clinicopathologic findings and prognosis – indicating great potential for the evaluation of both luminal and extraluminal masses in CCA diagnosis [13, 31, 32].

Intraductal US

Intraductal US (IDUS) is a valuable, albeit uncommonly used, imaging modality which can be easily performed during endoscopic retrograde cholangiopancreatography (ERCP) and is suitable for visualizing narrow ductal cavities such as the bile duct and pancreatic duct [33]. In recent years, some studies have indicated that IDUS has a significant role in distinguishing malignant bile duct obstructions from benign ones with a rate of accuracy of around 90% [33, 34].

Endoscopic US

Currently, endoscopic US (EUS) is recognized as an important tool for diagnosing pancreaticobiliary disease, which is helpful to display the morphology of a bile duct stricture clearly (such as any irregularity and its wall thickness), to stage regional lymph node and portal vein involvement and to facilitate diagnostic tissue acquisition [11]. An early study indicated that EUS had the same sensitivity and specificity in differentiating bile duct obstruction combined with ERCP, magnetic resonance cholangiopancreatography (MRCP), and CT [35]. EUS-guided fine needle aspiration (EUS-FNA) may establish the diagnosis of bile duct obstruction with a sensitivity for the diagnosis of malignancy ranging from 27 to 83%, indicating the potential value of preoperative evaluation for CCA [36].

It should be noted that gastrointestinal gas and obesity frequently obscure the distal bile duct, and the result of transabdominal US is significantly influenced by the experience of the ultrasonographer and the quality of the equipment. In addition, IDUS requires the addition of ERCP at the same sitting, and has inferior performance for staging regional adenopathy and evaluation after biliary stent placement [37]. Importantly, tissue acquisition with EUS-FNA from suspected malignant proximal biliary strictures has been reported to have the potential risk of tumor seeding along the needle track [36]. Besides, EUS-FNA is also operator dependent and difficult to perform widely.

Fig. 1. Contrast-enhanced computerized tomography images of a 50-year-old male with infiltrative distal common bile duct (CBD) cholangiocarcinoma. The images (arterial phase) show the annular thickening and obvious enhancement of the wall of the distal CBD (a, b, blue arrows), with the intrahepatic and extrahepatic bile ducts dilated (c, red arrow).

Computerized Tomography

Multi-detector CT, which is noninvasive and has high spatial resolution in multiple imaging planes, is widely available to detect hepatobiliary disease. Multi-detector CT, especially contrast-enhanced CT, has been commonly used for the characterization of liver masses; the detection of bile (Fig. 1) or pancreatic duct dilatation, stenosis, and vascular involvement; and the assessment of lymph nodes and distant metastases [38, 39]. Meanwhile, the use of multiple postprocessing techniques, such as multi-planar reconstruction, curved planar reformation, maximum intensity projection, and 3D volume rendered images, is critical to evaluate the craniocaudal extent of infiltrative or intraluminal polypoidal lesions [40].

Recent research has demonstrated that CT techniques can effectively differentiate between CCA and other diseases, such as hepatocellular carcinoma (HCC) [41], liver abscess [42], and liver metastases [43]. It has been reported that CT perfusion or contrast-enhanced CT may assist in the diagnosis and differential diagnosis of CCA, which could guide optimal clinical treatment strategies [44–46]. In addition, recent studies have shown that dual-energy CT was also used to evaluate CCA and for the differentiation between small ICC and small liver abscess, which provided a new method of quantitatively assessing CCA [47, 48].

CT techniques are also able to accurately calculate liver volume and residual liver volume, assisting in making an optimal individualized surgical plan, leading to shorter surgical durations and less intraoperative blood loss, improving the surgical success rate, and reducing the incidence of operative complications [49]. Furthermore, these techniques can help to retain as much of the liver volume as possible and to reduce the risk of postoperative liver failure [49]. Survival outcomes in surgical patients

can also be identified based on the qualitative imaging features of CCA on CT, resulting in a better prediction of prognosis [16].

However, some shortcomings in this modality are noteworthy. CT has ionizing radiation and may be harmful to overall patient health. Although CT can detect the dilation and stricture of bile ducts with a high degree of sensitivity, it has a weaker ability to evaluate the spread of the tumor along bile ducts and has a lower sensitivity for the preoperative evaluation of lymph node involvement than MRI [50].

PET Imaging

Positron Emission Tomography/Computerized Tomography

Fluorine-18 fluorodeoxyglucose PET CT (^{18}F -FDG PET/CT), a noninvasive imaging technique that allows in vivo assessment of the metabolic processes underlying malignant disease [51], is widely used in oncology imaging to diagnose and monitor the treatment response of cancer. To date, ^{18}F -FDG PET/CT has been widely used to evaluate multiple malignancies such as colorectal cancer [52], lung cancer [53], and breast cancer [54]. Various studies have indicated that ^{18}F -FDG PET/CT plays an important role in assessing CCA and have estimated the efficiency to detect and diagnose CCA at sensitivities of 84–94% and specificities of 79.3–100% [55, 56]. Also, PET/CT has the advantage of the detection of lymph node metastases (LNM) and distant metastases of CCA [17], with a sensitivity up to 100% in detecting distant metastases [57]. Meanwhile, PET/CT also excels at differentiating ICC from distal cholangiocarcinoma based on metabolic behavior, especially FDG uptake, having an advantage in predicting survival and prognosis [58].

Fig. 2. Images of a 43-year-old female with distal common bile duct cholangiocarcinoma (blue arrows). Axial T1-weighted imaging (a) and fat-suppressed T2-weighted imaging (b) demonstrate an intermediate signal of a soft-tissue nodule, with a high signal on axial diffusion-weighted imaging (c).

Color version available online

Of course, other tracers such as (11)C-choline and ^{68}Ga -prostate-specific membrane antigen have been also proven to be a promising method for assessing CCA, which may assist in the detection and finding of therapeutic options for CCA [59, 60].

However, PET/CT also has some limitations. First, it has a high cost and is not suitable for routine clinical examination. Second, PET alone is limited by poor temporal and spatial resolution with a somewhat restricted anatomic localization of positive lesions [40]. Finally, other limitations include misinterpretation of normal physiological activity of the bowel and genitourinary system and misregistration [40]. False-negative findings and false-positive results are possible with some lesions, leading to diagnostic obscurity [40, 61].

Positron Emission Tomography/Magnetic Resonance Imaging

In recent studies, ^{18}F -FDG PET/MRI has been attempted for discriminating the histopathologic subtypes and histological grades of hepatic tumors, which may help to differentiate CCA from other hepatic neoplasms and predict the differentiation degree (DD) of CCA [62, 63]. Besides, Ferrone et al. [64] investigated management implications of PET/MRI in patients with untreated ICC, discovering that PET/MRI significantly influenced the treatment strategy in part of patients with ICC. Two quantitative parameters, including the maximum standard uptake value and apparent diffusion coefficient, were obtained simultaneously to provide complementary information on hepatic tumors by using PET/MRI scanning, indicating that PET/MRI may be a useful tool for the diagnosis, as well as for gauging the aggressiveness and prognosis, of a tumor, including CCA.

Regrettably, like PET/CT, PET/MRI has still a high cost and shows some similar disadvantages. Moreover,

PET/MRI has longer scan times and more contraindications than PET/CT.

Magnetic Resonance Imaging

At present, MRI is considered the most accurate and least invasive imaging modality for the assessment of CCA (Fig. 2) [65]. MRI has the additional advantages of using no ionizing radiation, offering a high-quality soft-tissue contrast and tumor evaluation, as well as precise visualization of bile ducts and adjacent structures. These improvements are achieved through the combination of multiple sequences, including T1-weighted imaging [66], T2-weighted imaging [67], diffusion-weighted imaging (DWI) [21], MRCP [19], and dynamic contrast-enhanced MRI (DCE-MRI) [20, 65]. MRI techniques excel at visualizing malignant stricture with or without an associated mass, permit accurate lesion characterization, improve sensitivity in the evaluation of tumor extent along the bile duct and liver invasion, and provide staging information regarding vascular, ductal and lymph node status [68].

Although the ability of MRCP to differentiate the causes of structural disease is limited, and cannot alone be used in assessing resectability in most situations, it has been proven to be an optimal imaging modality for the evaluation of the biliary system, particularly excelling at assessing the tumor extent along the bile ducts [68] and visualizing the biliary ducts proximal to an obstruction [65]. Previous studies have documented that MRCP can differentiate benign from malignant causes of biliary obstruction [19] and assess the possibility of resectability [69].

It has been proven that DWI can increase the conspicuity of lesions, improving the diagnostic sensitivity of MRI for CCA [70]. It may also contribute to the differentiation between ICC (Fig. 3) and other hepatic malignancies, such as solitary hypovascular liver metastases [71]

Fig. 3. Images of a 54-year-old male with a segment VI intrahepatic cholangiocarcinoma (blue arrows). The lesion has a low signal on axial T1-weighted imaging (a), and a heterogeneous high signal on axial fat-suppressed T2-weighted imaging (T2WI) (b), axial diffusion-weighted imaging (c), and coronary non-fat-suppressed T2WI (d).

Fig. 4. Images of a 38-year-old man with a perihilar cholangiocarcinoma (blue arrows) invading the caudate lobe with intrahepatic bile duct dilatation. The tumor shows a slightly lower signal on axial T1-weighted imaging (a), an intermediate signal on axial fat-suppressed T2-weighted imaging (b), a high signal on axial diffusion-weighted imaging (c), and a low signal on the axial apparent diffusion coefficient (d).

and HCC (Fig. 4) [72]. Furthermore, DWI may serve as an independent tool to evaluate histopathologic findings and the prognosis of patients with CCA [73, 74]. It also allows a more accurate assessment of tumor status and the presence of associated satellite lesions when combined with DCE-MRI [75]. DCE-MRI may assist with a more accurate discrimination of intrahepatic mass-forming CCA from HCC [76] and improve prediction of the postoperative prognosis of intrahepatic mass-forming CCA [20].

Besides, intravoxel incoherent motion (IVIM) combined with DWI has been used to differentiate ICC from HCC, with the highest area under curve (AUC) of 0.803, suggesting that IVIM and DWI parameters can be useful in differentiating ICC from HCC and may be helpful in choosing a treatment plan and predicting prognosis [77, 78]. In another study, researchers predicted Ki-67 expression in CCA through IVIM and DWI (highest AUC = 0.880), which could reflect the proliferative activity of CCA and predict the degree of malignancy of the tumor to some extent [79].

One of the limitations to MRI is a long scanning time, which requires little to no patient movement. Many patients have difficulty remaining still enough to secure highest-quality images. In addition, some patients may not be suited for MRI due to contraindications, including patients with severe claustrophobia, intracranial aneurysm clips, cardiac pacemakers, cochlear implants, and other metals in their bodies [40].

Direct Cholangiography

Direct cholangioscopy, considered the standard of reference for evaluating the ductal extent of a tumor, allows the direct visualization of the biliary system and may help in the differentiation of unclear bile duct strictures [80]. ERCP and percutaneous transhepatic cholangiography are often required for the diagnosis and management of CCA, as tissue sampling and cytological and/or histological confirmation of the diagnosis are achievable by washing, brushing, or intraductal biopsy [23]. Cholangioscopic targeted biopsies of biliary lesions appear to improve the diagnostic yield and show accuracy rates of up to 90%

Fig. 5. Artificial intelligence methods in medical imaging. **a** Traditional flowchart of radiomics analysis, including segmentation of regions of interest (ROI), feature extraction, feature selection, and modeling. It relies on radiomics features extracted from ROI and conventional machine learning algorithms. **b** A new deep learning

algorithm, which also falls under radiomics but does not require region annotation. It consists of some hidden layers where radiomics feature extraction, selection, and ultimate modeling are performed simultaneously during training.

in detecting CCA [22]. More importantly, therapeutic drainage, as a valuable treatment modality for patients with CCA, also can be undertaken by using plastic or metal stents [80].

Both ERCP and percutaneous transhepatic cholangiography, however, are invasive, operator dependent, and associated with procedural risks, including duodenal perforation, biliary leakage, cholangitis, pancreatitis, and bleeding [80]. Besides, the sensitivity of these approaches remains limited. It has been reported that the sensitivity of transpapillary forceps biopsies in detecting malignant bile duct strictures ranges only from 43 to 81% [81]. In perihilar biliary obstruction, direct cholangiography frequently does not depict the ductal anatomic features proximal to occlusive lesions, especially in cases of high-grade obstruction [80].

AI in Medical Imaging

In recent years, AI techniques have resulted in many improvements across healthcare and have been used in many biomedical areas, especially focused on oncology (Fig. 5). AI, which plays an important role in the medical field, can be used for drug discovery, remote patient mon-

itoring, medical diagnostics and imaging, risk management, virtual assistance, and hospital management [24]. The major devices of AI consist of machine learning techniques and natural language processing methods [82]. Currently, large amounts of imaging data, coupled with data on clinical outcomes, have led to the emergence of AI within radiology and rapid development of radiomics as a new field of medical research [83].

Radiomics consists of the quantitative analysis of radiological images and machine learning methods [83]. The process extracts quantitative image features, also called “radiomics features,” to achieve richer information about the intensity, shape, size, volume, and texture of tumor phenotypes that are distinct from or complementary to information provided by clinical reports, laboratory test results, and genomic or proteomic assays [84]. Diagnostic, prognostic, and predictive models are then built through the integration of features extracted from large-scale radiological image modalities (e.g., MRI, CT, PET, and US) to support personalized clinical decisions and improve individualized treatment selection [85].

Recently, radiomics tools have been successfully explored to assist clinical decision-making related to the diagnosis and risk stratification of different cancers. For example, studies in gliomas have used radiomics to predict

the grading, molecular subtyping, and isocitrate dehydrogenase genotype, as well as low-grade glioma-related epilepsy, response to treatment, and the overall survival rate [86–89]. In addition, there are many related radiomics studies on non-small cell lung cancer that could predict distant metastasis in lung adenocarcinoma [90], histological tumor subtypes [91], disease recurrence [92], somatic mutations [93], gene expression profiles [94], and the overall survival rate [95]. Moreover, radiomics tools have also been applied to explore and evaluate other oncological foci, such as the prediction of immunohistochemical molecular classification in breast cancers [96], the differentiation of five liver masses [97], the prediction of complete response after neoadjuvant chemoradiation for locally advanced rectal cancer [98], and the preoperative prediction of LNM in bladder cancer [99]. It has been reported that radiomics approaches have also been applied to a number of non-oncological fields. The change in texture feature values between pre- and post-radiotherapy CT scans could be used to characterize radiation-induced damage to the lung [100]. Possible neurological applications include the diagnosis, staging, and prognosis of Alzheimer's and Parkinson's disease [101], as well as of multiple sclerosis [102]. In addition, the liver fibrosis stage could also be evaluated using a deep convolutional neural network [103]. The emerging field of radiomics has considerable potential in disease diagnosis, prognostic evaluation, and prediction of treatment response. AI can use sophisticated algorithms to extract and analyze features from a large volume of clinical and radiological data, and then use the obtained insights to guide clinical practice [82], assist in early detection and diagnosis, and make real-time inferences for health risk alerts and health outcome prediction of some diseases [83].

Application of AI in CCA

Although the role of AI in the evaluation of patients with CCA is not as established as routine imaging detection, AI is increasingly used in detecting and diagnosing CCA.

A previous paper demonstrated that an artificial neural network (ANN) was designed to differentiate four hepatic masses (HCC, intrahepatic peripheral CCA, hemangioma, and metastasis), reporting that the average AUC for ANN alone was 0.961. The ANN had the capability to differentiate some hepatic masses by use of CT and could improve the diagnostic accuracy of radiologists [104]. In another study, a popular ANN, the multi-layer

perceptron, was used for differentiating images with CCA from those without. As a result, the achieved test was 94% correct when differentiating only healthy from tumor images, and 88% correct in a robust multi-disease test, indicating that using a multi-layer perceptron can accurately detect CCA in 2D MRCP images [25]. Pattanapairoj et al. [26] constructed a classification model using both C4.5 (which is an algorithm used to construct a decision tree classification model in a logical form) and an ANN to improve the discriminatory ability of certain serum markers for the diagnosis of CCA.

In a recent retrospective study, researchers discovered that certain texture parameters correlate significantly with epidermal growth factor receptor and vascular endothelial growth factor expression levels, suggesting that radiogenomic methods may predict protein expression of CCA and have a potential impact on therapy [27]. In addition, a novel radiomics nomogram based on radiomics signatures and clinical characteristics can be used to preoperatively predict early recurrence of ICC after partial hepatectomy, resulting in devising appropriate strategies, which benefits patients with a high risk of early recurrence who need additional chemotherapy [28]. This result is best shown in a study, comprising a total of 288 patients, in which Shao et al. [105] constructed an ANN model to accurately predict early occlusion of bilateral plastic stent placement for inoperable HCC, which is critical in treatment selection for patients with inoperable CCA. In a recent study, Ji et al. [106] established and validated a radiomics model for predicting LNM of ICC and determined its prognostic value, with good calibration and discrimination in the primary cohort (AUC = 0.8462) and the validation cohort (AUC = 0.8921). Similarly, a radiomics model derived from portal-phase CT of the liver was developed to predict LNM and survival outcomes in biliary tract cancer, with an AUC of 0.81 and 0.80 in the primary cohort and the validation cohort, respectively. In other words, a noninvasive and convenient radiomics model that incorporates the radiomics signature and CT-reported lymph node status may facilitate clinical decision-making and potentially improve survival outcomes in selected patients [107].

In a recent study, a radiomics approach based on a support vector machine (SVM) using MRI was used to preoperatively evaluate LNM in ICC. The combination nomogram based on the SVM score, the CA19-9 level, and the MR-reported LNM factor showed better discrimination than the SVM model alone (AUC for the training group: 0.842 vs. 0.788; AUC for the validation group: 0.870 vs. 0.787) [108]. Another study consisted of

Table 1. Different applications of AI in CCA

First author [Ref.]	Year	Images	Methods	Subjects, <i>n</i>	Purpose	AUC
Matake et al. [104]	2006	CECT	ANN	120	To evaluate the performance of ANN for differential diagnosis of hepatic masses, including CCA	0.961
Logeswaran [25]	2009	MRCP	MLP	648	To differentiate images with CCA from those without	–
Pattanapairoj et al. [26]	2015	No	C4.5, ANN	85	To improve the diagnostic power of serum markers using C4.5 and ANN	–
Sadot et al. [27]	2015	CECT	Multiple linear regression analysis	56	To investigate associations between imaging features of CCA and texture analysis	–
Liang et al. [28]	2018	CECT	LASSO	209	To develop a novel radiomics nomogram for predicting ER of ICC	0.90
Shao et al. [105]	2018	No	BP-ANN	288	To predict early occlusion of bilateral plastic stent placement for inoperable HCC	0.9648
Ji et al. [106]	2019	CECT	LASSO	103	To develop a radiomics model for predicting LNM of ICC and to determine its prognostic value	0.9244
Ji et al. [107]	2019	CECT	LASSO	247	To evaluate a radiomics model for predicting LNM in BTCs and to determine its prognostic value	0.81
Xu et al. [108]	2019	MRI	SVM	148	To develop a prediction model for preoperative LNM in ICC patients	0.870
Peng et al. [109]	2019	US	LASSO, SVM	128	To develop radiomics signatures based on US to assess the biological behaviors of ICC	0.930
Yang et al. [110]	2020	MRI	Random forest	100	To evaluate diagnostic performance of radiomics models of MRI in the detection of DD and LNM of ECC	0.90

The AUC values in the table were the best results in the above studies. AI, artificial intelligence; AUC, area under the curve; ANN, artificial neural network; CECT, contrast-enhanced computerized tomography; CCA, cholangiocarcinoma; MRCP, magnetic resonance cholangiopancreatography; MLP, multi-layer perceptron; C4.5, an algorithm used to construct a decision tree classification model in a logical form; ER, early recurrence; ICC, intrahepatic cholangiocarcinoma; LASSO, least absolute shrinkage and selection operator; BP-ANN, back-propagation artificial neural network; HCC, hilar cholangiocarcinoma; LNM, lymph node metastasis; BTCs, biliary tract cancers; SVM, support vector machine; MRI, magnetic resonance imaging; US, ultrasound; DD, differentiation degree; ECC, extrahepatic cholangiocarcinoma.

128 ICC patients' established and validated radiomics signatures based on US images to assess the biological behavior of ICC in a noninvasive manner, providing a novel approach to precision medicine for ICC patients [109]. Furthermore, in our previous study, we evaluated the diagnostic performance of radiomics models of MRI in the detection of DD and LNM of extrahepatic cholangiocarcinoma (ECC) through random forests, discovering that the radiomics models showed better performance in both the training and the testing cohort in predicting DD and LNM of ECC, with the highest AUC reaching 0.90. The above results suggest that the radiomics models based on MRI performed well in predicting DD and LNM of ECC and have significant potential in clinical noninvasive diagnosis and in the prediction of ECC [110] (Table 1).

As we all know, the diagnosis or differential diagnosis of CCA or other tumors is sometimes difficult and

requires much experience and knowledge because of the variety in radiological features of each disease and the overlap of radiological findings between many diseases [105]. Within the present detection workflow, radiologists are usually trained to identify abnormalities on the basis of changes in imaging intensities or the appearance of unusual patterns, relying on subjective perceptive and cognitive skills [24]. However, in contrast to such qualitative evaluation, AI can recognize complex patterns in imaging data and provide a quantitative and objective assessment of tumors automatically. Moreover, a more accurate and reproducible radiological assessment can be achieved with the integration of AI into the clinical workflow [24]. Therefore, we can evaluate CCA more accurately by combining AI with imaging to determine clinical management and prognostic evaluation.

Conclusions

CCA is still a malignant neoplasm with an extremely unfavorable prognosis. Recent advances in imaging techniques have led to improved detection, characterization, and pre-treatment staging of these lesions, which in turn guides clinicians to make optimal therapeutic strategies. Our vision for the application of AI in CCA is expansive and bold. We expect that AI analysis is not only restricted to retrospective, single-center, and small-sample studies. More significantly, prospective multicenter studies with large data sets are needed to further predict CCA, including pathology, prognosis, treatment, and so on. Meanwhile, some clinical, pathological, radiological, and even genomic features should be considered in the analysis of AI for CCA besides for images.

For the immediate future, AI, especially in the field of imaging, will focus on the creation of suitable infrastructures to facilitate the development and validation of models. We envision that AI, a novel technique, will facilitate the diagnosis, prognosis, and treatment of CCA, resulting in improved personalization and precision medicine. Moreover, picture archiving and radiomics knowledge systems of the future may identify, segment, and extract features from regions of interest, not only for evaluating CCA. In summary, AI is at its very early stages in CCA

and many challenges need to be addressed. We believe that simultaneous and synergistic advances in imaging and AI will empower the next major breakthroughs in personalization and precision medicine.

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Conflict of Interest Statement

The authors of this manuscript declare no relationships with any companies whose products or services may be related to the subject matter of the article.

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Author Contributions

Literature search and manuscript preparation: Chun Mei Yang; study concept and design and manuscript editing: Jian Shu.

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