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Artificial Intelligence in Upper Gastrointestinal Endoscopy

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Keywords

Artificial intelligence · Deep learning · Esophageal cancer · Gastric cancer · Endoscopy

Abstract

Background: Over the past decade, several artificial intelligence (AI) systems are developed to assist in endoscopic assessment of (pre-)cancerous lesions of the gastrointestinal (GI) tract. In this review, we aimed to provide an overview of the possible indications of AI technology in upper GI endoscopy and hypothesize about potential challenges for its use in clinical practice. ***Summary:*** Application of AI in upper GI endoscopy has been investigated for several indications: (1) detection, characterization, and delineation of esophageal and gastric cancer (GC) and their premalignant conditions; (2) prediction of tumor invasion; and (3) detection of *Helicobacter pylori*. AI systems show promising results with an accuracy of up to 99% for the detection of superficial and advanced upper GI cancers. AI outperformed trainee and experienced endoscopists for the detection of esophageal lesions and atrophic gastritis. For GC, AI outperformed mid-level and trainee endoscopists but not expert endoscopists. ***Key Messages:*** Application of artificial intelligence (AI) in upper gastrointestinal endoscopy may improve early diagnosis of esophageal and gastric cancer and may enable endoscopists to better identify patients eligible for endoscopic resection. The benefit of AI on the quality of upper endoscopy still needs to be demonstrated, while prospective trials are needed to confirm accuracy and feasibility during real-time daily endoscopy.

Introduction

Accurate endoscopic detection of esophageal and gastric cancers and their premalignant conditions, such as Barrett neoplasia, gastric atrophy, and intestinal metaplasia, is essential for the detection of these cancers at an early stage [1–4]. The challenge of endoscopic procedures lies in the real-time interpretation of endoscopic imagery, which is complex and sensitive to human error. Current endoscopic cancer screening and surveillance strategies encounter several pitfalls, including interobserver variability in the detection of lesions, time-consuming biopsy protocols, and biopsy sampling error [1, 5, 6]. Especially subtle and early (pre-)malignant lesions in the esophagus and stomach can easily be missed by endoscopists (Fig. 1).

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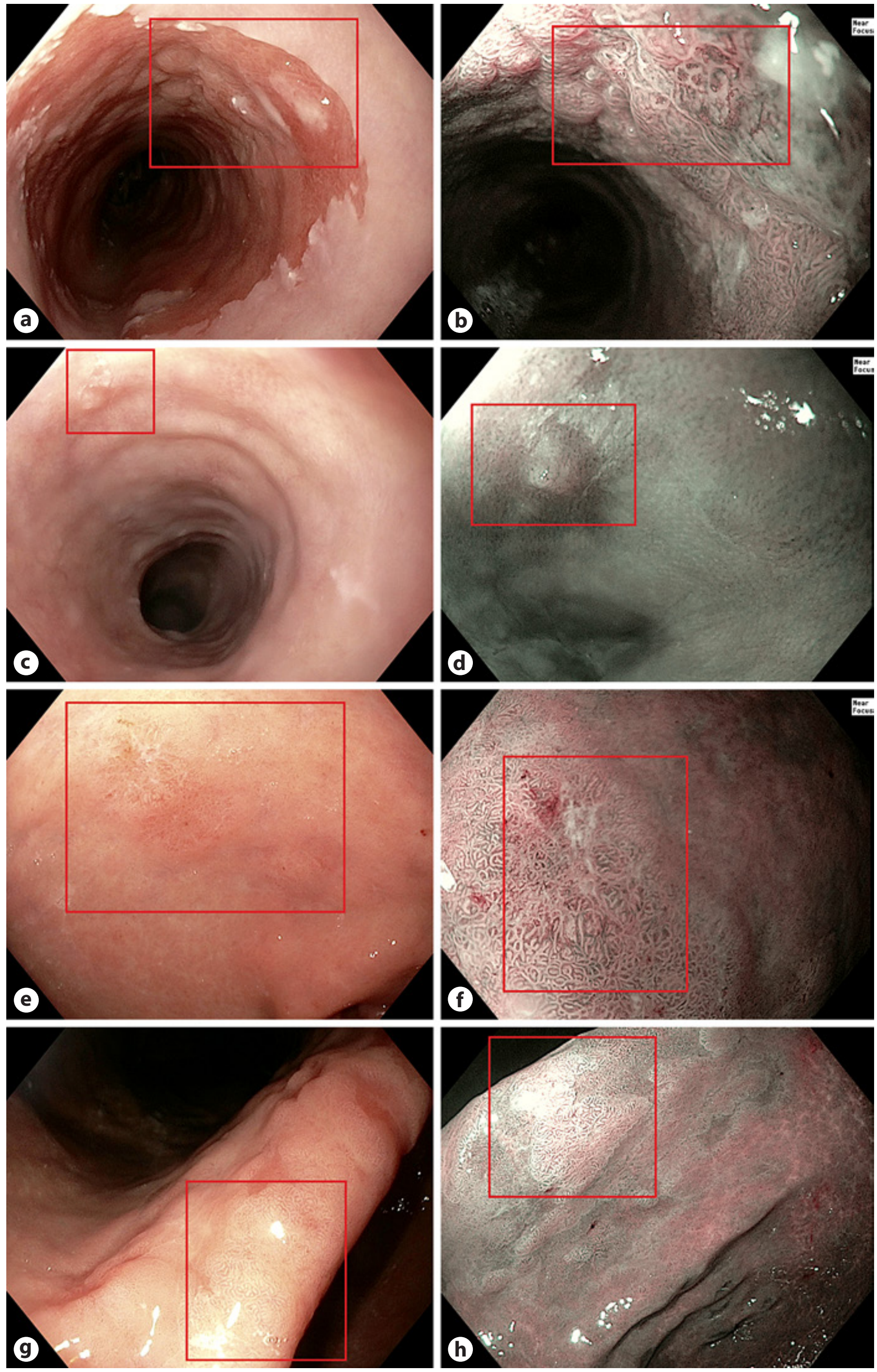

Fig. 1. Endoscopic images of subtle early esophageal and gastric (pre-)malignant lesions of which detection rates can be increased with assistance of AI. The (pre-)malignant lesions are marked with a red rectangle. **a** Early BE neoplasia with WLE. **b** The same lesion as **a** with ME-NBI. **c**, **d** ESCC with WLE and ME-NBI. **e**, **f** EGC with WLE and ME-NBI. **g**, **h** GIM located at the angulus in the stomach with WLE and NBI. AI, artificial intelligence; BE, Barrett's esophagus; EGC, early gastric cancer; ESCC, esophageal squamous cell carcinoma; GI, gastrointestinal; GIM, gastric intestinal metaplasia; ME, magnified endoscopy; ME-NBI, magnified endoscopy and narrow band imaging; NBI, narrow band imaging; WLE, white light endoscopy.

Artificial intelligence (AI) technology has the potential to overcome these obstacles. AI models have been introduced as a tool to aid in endoscopic detection, characterization, and delineation of premalignant and malignant lesions of the upper gastrointestinal (GI) tract [7–11]. Over the past decade, several AI systems have been developed to assist endoscopists in the detection and staging of lesions in the upper GI tract. In this review, we aimed to provide an overview of the possible indications of AI systems in upper GI endoscopy (shown in Fig. 2) and hypothesize about potential challenges for its use in clinical practice.

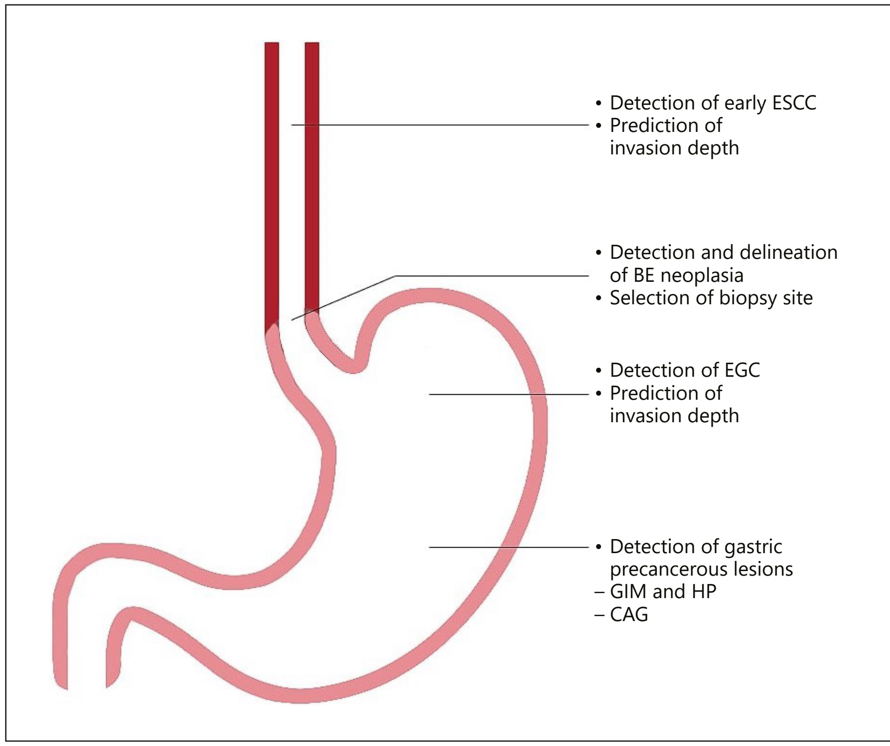

Fig. 2. Application of AI in upper GI endoscopy – topics that are addressed in this review. AI, artificial intelligence; BE, Barrett's esophagus; CAG, chronic atrophic gastritis; EGC, early gastric cancer; ESCC, esophageal squamous cell carcinoma; GI, gastrointestinal; GIM, gastric intestinal metaplasia; HP, *Helicobacter pylori*.

Principles of AI

AI refers to a machine-based intelligence which mimics human cognitive functions, such as learning and decision-making. Machine learning (ML) is a form of AI consisting of a teaching algorithm to recognize data patterns and utilize data to predict new data. In order to predict outcomes, an ML algorithm needs to be exposed to different example datasets. Deep learning (DL) is an advanced ML method, which uses layers of artificial neural networks to hierarchically structure data and extract features without human aid. Similar to the human brain, DL methods approach tasks by analyzing information from different concepts before assigning them to a specific class. Different from conventional ML algorithms that need human intervention to correct errors, DL has the ability to learn from its mistakes. This self-learning ability of DL technology makes it possible to increase its performance as exposure to data increases.

The most widely known DL method in endoscopy is based on convolutional neural network (CNN) and consists of a neural network architecture which is mainly used for image recognition and classification. To achieve sufficient diagnostic accuracy, a DL system needs to be trained and validated with large amounts of labeled data during different steps (shown in Fig. 3). First, the algorithm is subjected to a large dataset of mostly nonendoscopic labeled images. These labeled images are often obtained from open access databases, such as ImageNet [12]. Second, the algorithm needs to be trained and validated with a dataset of labeled endoscopic images. Last, when performance is sufficient, the algorithm needs to be tested. Computer-aided detection (CAD) systems in GI endoscopy are ML methods specifically developed to assist endoscopists to improve accurate detection and staging of pathology, including early stages of disease and selection of optimal biopsy sites.

Esophagus

Neoplasia in Barrett's Esophagus

The incidence of esophageal adenocarcinoma (EAC) is rapidly increasing in Western society [13, 14]. Barrett's esophagus (BE) is a precancerous condition, which may progress to EAC [15]. Therefore, guidelines recommend endoscopic surveillance of BE in order to diagnose neoplastic progression in early stages. Endoscopic assessment of the esophagus with high-definition (HD) white light endoscopy (WLE) is advised to optimize the detec-

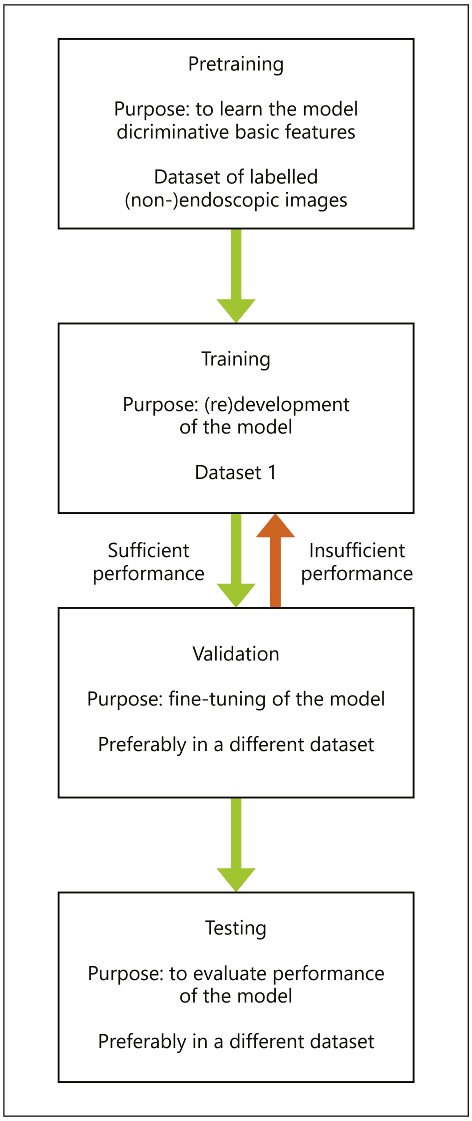

Fig. 3. Visual steps in the development of an AI model: pretraining, training, validation, and testing. AI, artificial intelligence.

tion of dysplastic Barrett mucosa [1, 2]. Chromoendoscopy can be utilized to aid in detection of lesions; however, additional value to WLE has not been proven [16]. Given the low progression rate among BE patients, which is estimated at 0.5% per year, the majority of gastroenterologists never encounter dysplasia and therefore may be less familiar with the mucosal changes associated with presence of neoplasia [17]. Visible neoplastic lesions, including early EAC, may remain undetected, especially when endoscopic surveillance is performed by endoscopists with limited experience in the recognition of early neoplastic lesions [18, 19]. Low-grade dysplasia may present itself with very subtle mucosal changes and is therefore easily missed [6]. To increase the diagnostic yield of dysplasia, guidelines recommend taking 4-quadrant biopsies at each 2-cm interval of the Barrett segment, known as the Seattle protocol [20]. Combined with WLE, it is estimated that up to 90% of high-grade dysplasia (HGD) and EAC cases are detected [21]. Nevertheless, adherence to this protocol is poor as it is a time-consuming procedure, especially in patients with a long-segment BE [22].

AI in the Detection of Barrett Neoplasia

Several ML methods were developed to aid in diagnosis of BE neoplasia (Table 1). The majority of studies evaluated diagnostic performance of CNN algorithms in WLE images [7, 10, 23–27]. Hashimoto et al. [25] developed an algorithm based on CNN technology to aid in the detection of Barrett neoplasia by image annotation of areas suspect for neoplasia. The pretrained algorithm was trained with 916 images of BE patients with HGD and early EAC. The CNN then analyzed 225 images of dysplastic BE and 233 of nondysplastic Barrett's esophagus (NDBE) images with 95% accuracy. The ARGOS consortium performed several studies with AI algorithms to aid in the detection, characterization, and delineation of BE neoplasia and to improve the selection of biopsy sites [7, 23, 27, 28]. De Groof et al. [7] developed an AI model based on prospectively collected WLE images for the detection and delineation of BE neoplasia with a sensitivity, specificity, and accuracy of 95%, 85%, and 92%, respectively. Application of CAD in detection of Barrett neoplasia is also being explored in NBI images and videos [25, 26, 28]. Struyvenberg et al. [28] developed a CAD system using 30,021 NBI video frames (average video consisted of 250 fragments obtained during 10 s of video) and detected BE neoplasia with accuracy of 83%.

Recently, the first prospective studies during live endoscopic procedures were performed by de Groof et al. [24] and Ebigbo et al. [10]. De Groof et al. [23] trained their CAD model with 1,704 high-resolution images of 669 patients with histologically confirmed Barrett neoplasia or NDBE. Algorithm performance was externally validated with separate datasets, each containing 80 images which were also scored for the presence of dysplasia by 53 general endoscopists. The CAD system classified images as dysplastic or nondysplastic with 90% sensitivity, 88% specificity, and 89% accuracy. The AI model outperformed the endoscopists in detection of early Barrett neoplasia in another dataset containing 80 images as the sensitivity, specificity, and accuracy of the CAD system

Table 1. Application of AI in the detection of BE neoplasia

Author	Country	Study design	Aim	Modality	AI model			Endoscopists			
					Sens %	Spec %	accuracy %	experience, years	Sens %	Spec %	accuracy %
Ebigbo et al. [10]	Germany	Pro	Detection of BE neoplasia during live endoscopy	WLE	84	100	90	x	x	x	x
de Groof et al. [23]	Netherlands	Retro	Detection of BE neoplasia	WLE	93	83	88	Seniors >5 Juniors <3 Fellows Novices	77 79 71 60	73 76 76 72	75 78 73 66
de Groof et al. [24]	Netherlands	Pro	Detection and delineation of BE neoplasia and selection of optimal biopsy site during live endoscopy	WLE	91	89	90	x	x	x	x
Hashimoto et al. [25]	USA	Retro	Detection and image annotation of BE neoplasia	WLE/ ME-NBI	96	94	95	x	x	x	x
Ebigbo et al. [26]	Germany	Retro	Detection of BE neoplasia	WLE NBI	92–97 94	88–100 80	x	x	76 99	80 78	x
de Groof et al. [7]	Netherlands	Pro data collection	Detection and delineation of BE neoplasia	WLE	95	85	92	x	x	x	x
van der Sommen et al. [27]	Netherlands	Retro	Detection and delineation of BE neoplasia	WLE	86	87	x	Experts*	95–100	73–93	x

AI, artificial intelligence; BE, Barrett's esophagus; ME, magnified endoscopy; NBI, narrow band imaging; NDBE, nondysplastic Barrett's esophagus; Pro, prospective; Retro, retrospective; Sens, sensitivity; Spec, specificity; WLE, white light endoscopy; x, not reported. * Years of experience (of subgroups) of endoscopists unknown.

and endoscopists was, respectively, 93% versus 72%, 83% versus 74%, and 88% versus 73% [23]. The CAD model was tested during real-time endoscopy with an accuracy of 90% [24]. Ebigbo et al. [26] developed a CAD-DL system based on 148 HD-WLE and NBI images of 33 early EAC and 41 NDBE areas in one database and 100 HD-WLE images of 17 early EAC and 22 NDBE areas in a second database. Based on the images in these two datasets, the AI model reached a 92–97% sensitivity and 88–100% specificity for WLE images and 94% sensitivity and 80% specificity for NBI images. Afterwards, the developed CNN-CAD algorithm was tested during real-time daily endoscopy in 14 patients with BE neoplasia with an accuracy of 89.9% [10]. The majority of previous mentioned studies showed high accuracy of AI models in the detection of BE neoplasia. Main limitations of these studies were the retrospective design and small sample size.

Esophageal Squamous Cell Carcinoma

Squamous cell carcinoma remains the predominant histologic type of esophageal cancer (EC), which accounts for 80% of the cases worldwide [29, 30]. The incidence rates of esophageal squamous cell carcinoma (ESCC) vary strongly among geographic regions, with highest rates in Eastern Asia [29]. Most ESCC are detected in advanced stages and therefore associated with a poor 5-year survival rate of merely 20% [31]. The prognosis of early ESCC is considerably better, since the risk of lymph node and distant metastasis is associated with the tumor invasion depth [32]. Additional lugol's iodine staining or WLE and NBI can be used to increase the detection of subtle esophageal lesions [33, 34]. The combination of magnification and NBI during endoscopy (ME-NBI) allows visualization of the microvasculature of the esophageal epithelium, which can be classified according to the intrapapillary capillary loop (IPCL) classification [35]. This classification can help differentiate dysplasia from nondysplasia in daily clinical practice [36].

AI in the Detection of ESCC

Most studies that investigated AI for the early detection of ESCC derive from Asian countries [29, 37–43]. AI models based on CNN during WLE are mostly investigated to detect squamous dysplasia and early ESCC (shown in Table 2) [37–41]. Horie et al. [9] developed a CNN-CAD system for the detection of EC (both ESCC and EAC; 8,428 images for system development and 1,118 images for validation). This study showed that CNN-CAD can correctly detect EC cases, including both superficial and advanced cancers with a sensitivity of 98%. Furthermore, the CNN-CAD system was accurately able to detect small cancerous lesions <10 mm that can be easily missed, even by experienced endoscopists. Shimamoto et al. [41] compared the use of DL during WLE and during NBI for the accurate detection of the invasion depth in ESCC. The accuracy was higher in WLE than that in ME-NBI (98.7% vs. 89.2%) [41]. Ohmori et al. [37] showed that their AI system had a high sensitivity for the detection of ESCC using non-ME NBI and high accuracy for the differentiation of ESCC from noncancerous lesions.

Endoscopic screening and detection of ESCC remains challenging partly because it is liable to the interobserver variability between endoscopists [35]. Early-stage ESCC are difficult to detect, especially for trainee endoscopists (sensitivity of NBI for ESCC detection in trainee vs. expert endoscopists: 53% vs. 100%) [45]. Several studies compared diagnostic parameters of developed AI models to endoscopists [37–42, 44]. Cai et al. [38] developed a CNN-CAD system based on WLE (2,428 images from 746 patients for training and 187 images from 52 patients for validation) which was compared to 3 groups of endoscopists (seniors with >15 years of experience, mid-levels with 5–15 years of experience, and juniors with <5 years of experience). Sensitivity of AI for detection of ESCC appeared to be higher, even for the experienced endoscopists. The sensitivity of the AI system versus senior, mid-level, and junior endoscopists was 97.8% versus 86.3%, 78.6%, and 61.9%, respectively. Zhao et al. [42] developed a CAD model based on ME-NBI to investigate the automated classification of IPCLs. The mean diagnostic accuracy of the CAD system was higher than that of mid-level and junior endoscopists for the detection of malignant esophageal lesions ($p < 0.001$). Fukuda and colleagues [44] divided the diagnostic process into 2 parts: detection (identify suspicious lesions) and characterization (differentiate cancer from no cancer). The developed CNN-DL system had a better diagnostic performance than the expert endoscopists [44]. Major limitations of these studies included the small sample size of images used for both training [38, 42] and validation [37, 38, 42, 44]. Furthermore, the samples of participating endoscopists with different levels of endoscopic experience were relatively small, ranging from 4 to 15 endoscopists per subgroup.

AI in Prediction of Invasion Depth of ESCC

The tumor invasion depth is an important prognostic factor in ESCC [46]. Accurate endoscopic detection of the invasion depth is essential for decision-making between endoscopic resection or proceeding to esophagectomy with lymphadenectomy [47]. To optimize endoscopic

Table 2. Application of AI in the detection of ESCC and prediction of invasion depth

Authors	Country	Study design	Aim	Modality	AI model			Endoscopists			
					Sens %	Spec %	accuracy %	experience, years	Sens %	Spec %	accuracy %
Guo et al. [43]	India	Retro	Detection of ESCC	NBI images videos	98 100	95 91	x	x	x	x	x
Ohmori et al. [37]	Japan	Retro	Detection of ESCC and differentiation ESCC versus no cancer	WLE ME-NBI/BLI	90 98	76 56	81 77	8–24	87 83	67 70	75 76
Fukuda et al. [44]	Japan	Retro	Detection of ESCC and differentiation ESCC versus no cancer	NBI/BLI	91	51	63	8–23	74–79	72–76	75
Tokai et al. [40]	Japan	Retro	Detection of ESCC and prediction of invasion depth	WLE	84	73	81	Unknown	79	62	74
Shimamoto et al. [41]	Japan	Retro	Prediction of invasion depth of ESCC	WLE ME-NBI/BLI	87 71	50 95	99 89	7–25	45 42	97 97	85 84
Cai et al. [38]	China	Retro	Detection of ESCC	WLE	98	85	91	>15 5–15 <5	86 79 62	91 84 92	89 82 77
Zhao et al. [42]	China	Retro	Feasibility of automated IPCL classification	ME-NBI	87	84	89	>15 10–15 5–10	91 79 68	84 71 76	92 82 73
Nakagawa et al. [39]	Japan	Retro	Prediction of invasion depth of ESCC	WLE	90	96	90	9–23	89	88	90

AI, artificial intelligence; BLI, blue light imaging; ESCC, esophageal squamous cell carcinoma; IPCL, intrapapillary capillary loop; Retro, retrospective; ME, magnified endoscopy; NBI, narrow band imaging; Sens, sensitivity; Spec, specificity; WLE, white light endoscopy; x, not reported.

prediction of invasion depth, the role of AI was studied [39–41]. Shimamoto et al. [41] developed an AI system on WLE and NBI images from endoscopic videos to estimate the invasion depth, which was compared to experienced endoscopists (7–25 years of experience). The AI model outperformed the endoscopists in both non-ME and ME-NBI with a sensitivity, specificity, and accuracy of AI versus endoscopists using ME-NBI of 71%, 95%, and 89% versus 42%, 97%, and 84%, respectively. Tokai and colleagues [40] developed an AI model to predict the ESCC invasion depth on 1,751 images, which was validated on 291 images. The diagnostic accuracy of the AI model outperformed 12 out of 13 endoscopists [40].

Stomach

Gastric Precancerous Lesions and Early Gastric Cancer

Helicobacter pylori (HP) infection can cause chronic atrophic gastritis (CAG) and gastric intestinal metaplasia (GIM), which are both precancerous conditions associated with an increased risk of gastric cancer (GC) development [3, 48]. GC is often diagnosed in an advanced stage, with an estimated 5-year survival rate of 20% [30]. Endoscopic surveillance is offered to patients with CAG and GIM to detect GC in an early stage as detection of early GC (EGC) improves survival [3]. Current surveillance strategies consist of adequate inspection of the gastric mucosa and standardized random biopsy sampling according to the Sydney protocol for topographic mapping [3]. Guidelines recommend use of HD-chromoendoscopy in GC surveillance as it improves optical diagnosis of precancerous lesions and EGC [3, 49–51]. The treatment strategy is determined by the invasion depth, which is an important prognostic factor in EGC [3, 30]. In early cases, diagnosis of EGC can be difficult as features can be subtle and EGC is easily missed in the presence of other pathology such as gastritis. AI models may improve the diagnostic accuracy by locating areas suspect for cancer and aid the endoscopist in detection and staging of gastric pathology.

AI in the Detection of EGC

The application of AI for the detection of EGC has been investigated in WLE images [52–57] and optic chromoendoscopy images (Table 3) [8, 58–63]. Li et al. [8] developed a CNN model on 386 images of benign lesions and 1,702 images of EGC for model development and 171 images of noncancerous lesions, and 170 EGC images to test the models' performance. The AI model had a diagnostic accuracy of 91% versus 87% when used by experts and 70–74% for nonexpert endoscopists. Horiuchi et al. [59] tested a CAD system to detect EGC using 174 NBI videos that contained 87 cancerous lesions. The CAD system was trained with 2,570 images containing cancerous and noncancerous gastric lesions. The performance of the CAD system was benchmarked against 11 endoscopists with experience in NBI and showed varying results. Only 2 endoscopists were outperformed by the CAD system. Similar results were found in the study of Ikenoyama et al. [55] that assessed the application of AI in detecting GC with both WLE and NBI.

AI in Prediction of Invasion Depth of EGC

Few research groups have developed CAD systems to assess the invasion depth of EGC [52, 56, 60]. Nagao et al. [60] developed a CNN-CAD system by using 16,557 images of 1,084 GC cases that underwent endoscopic resection or radical surgery, to study if invasion depth of EGC can be determined. Prediction of invasion depth was analyzed in both WLE and NBI modality. The CAD system predicted the invasion depth with a sensitivity of 84% and 75%, specificity of 99% and 100%, and accuracy of 94% and 94% during WLE and NBI images, respectively. Yoon et al. [52] analyzed 11,539 images of both GC (T1a and T1b) and non-EGC and predicted the invasion depth with an AUC of 0.85. However, in case of undifferentiated histology, the accuracy of the AI model was significantly lower. Despite the high performance of the CAD systems, only images were used to train and calculate performance of the algorithm, and video analysis has yet to be tested.

AI in Detection of Gastric Precancerous Lesions and HP Infection

Recent AI systems developed to enhance endoscopic detection of gastric precancerous lesions and HP are shown in Table 4 [11, 64–71]. In 2 studies, AI models were compared to endoscopists with different levels of experience in detection of CAG [11, 64]. Zhang et al. [64] designed a CNN model to detect CAG by using 5,470 antrum images of 1,699 patients. Images were classified as mild, moderate, and severe CAG. CAG was histologically confirmed in 3,042 images. The performance of the CNN model was compared to 3 expert endoscopists. The model outperformed the endoscopists with a sensitivity, specificity, and accuracy of 95%, 94%, and 94%, respectively. Highest detection rate was seen in severe CAG, with an accuracy of 99%. Guimarães et al. [11] showed similar results and reported a 93% accuracy for the detection of CAG in WLE images of the proximal stomach. Yan and colleagues [65]

Table 3. Application of AI in the detection of EGC and prediction of invasion depth

Authors	Country	Study design	Aim	Modality	AI model			Endoscopists			
					Sens %	Spec %	accuracy %	experience (EGDs, *n*), years	Sens %	Spec %	accuracy %
Ikenoyama et al. [55]	Japan	Retro	Detection of EGC	WLE/NBI	58	87	x	Mean 18.6 Mean 8.2	37 27	97 97	x
Ueyama et al. [58]	Japan	Retro	Detection of EGC	ME-NBI	98	100	99	x	x	x	x
Horiuchi et al. [59]	Japan	Retro	Detection of EGC Differentiation EGC versus gastritis	ME-NBI	87 95	83 71	85 85	>10 5–10	54–94 68–85	62–95 89–99	58–92 78–88
Nagao et al. [60]	Japan	Retro	Prediction of invasion depth of EGC	WLE NBI	84 75	99 100	94 94	x	x	x	x
Li et al. [8]	China	Retro	Detection of EGC	ME-NBI	91	91	91	>10 3	78–81 74–78	94–95 62–73	87 70–74
Cho et al. [54]	China	Retro	Detection of EGC Differentiation EGC versus precancerous lesions	WLE	28 50	88 91	75 76	Mean 6.7	69–93	87–100	82–98
Wu et al. [53]	Japan	Retro	Detection of EGC	WLE	94	91	93	Expert* Senior Trainee	94 90 75	87 85 89	90 87 81
Yoon et al. [52]	Korea	Retro	Detection of EGC Prediction of invasion depth	WLE	91 79	98 78	AUC 0.98 AUC 0.85	x	x	x	x
Zhu et al. [56]	USA	Retro	Prediction of invasion depth of EGC	WLE	76	96	89	>5,000 EGDs 2,000–5,000 EGDs	87 63	70 62	77 66
Hirasawa et al. [57]	Japan	Retro	Detection of EGC	WLE	92	x	92	x	x	x	x
Kanesaka et al. [61]	Taiwan	Retro	Detection and delineation of EGC	ME-NBI	97	95	96	x	x	x	x
Miyaki et al. [62, 63]	Japan	Retro	Detection of EGC Differentiation EGC versus no cancer	FICE	85	87	86	x	x	x	x

AI, artificial intelligence; AUC, area under the curve; BLI, blue light imaging; EC, esophageal cancer; EGC, early gastric cancer; FICE, flexible spectral imaging color enhancement; ME, magnified endoscopy; NBI, narrow band imaging; Retro, retrospective; Sens, sensitivity; Spec, specificity; WLE, white light endoscopy; x, not reported. * Years of experience of subgroups of endoscopists unknown.

Table 4. Application of AI in the detection of gastric precancerous lesions and HP

Author	Country	Study design	Aim	Modality	AI model			Endoscopists			
					Sens %	Spec %	accuracy %	experience (EGDs, *n*), years	Sens %	Spec %	accuracy %
Zhang et al. [64]	China	Retro	Detection of CAG	WLE	95	94	94	Experts* Trainee	88–92 60–62	90–91 58–60	89–92 59–61
Guimarães et al. [11]	Germany	Retro	Detection of CAG	WLE	100	88	93	>1,500 EGDs <1,500 EGDs	64 96	89 71	79 81
Yan et al. [65]	China	Retro	Detection of GIM	(ME-)NBI	92	86	89	10	87	81	84
Yasuda et al. [66]	Japan	Retro	Detection of HP infection	NBI	90	86	88	Expert* Endoscopist Senior resident	93 90 93	89 92 83	91 90 87
Zheng et al. [67]	China	Retro	Detection of HP infection	WLE	92	99	94	x	x	x	x
Shichijo et al. [68]	Japan	Retro	Detection of HP infection	WLE	x	x	80	x	x	x	x
Nakashima et al. [69]	Japan	Pro data collection	Detection of HP infection	WLE NBI	67 97	60 83–87	AUC 0.66 AUC 0.96	x	x	x	x
Itoh et al. [70]	Japan	Retro	Detection of HP infection	WLE	87	87	AUC 0.96	x	x	x	x
Huang et al. [71]	Taiwan	Retro	Detection gastric precancerous lesions and HP infection	WLE	85	91	85	Experts* Trainee	x	x	74–81 65–73

AI, artificial intelligence; AUC, area under the curve; CAG, chronic atrophic gastritis; EGD, esophagogastroduodenoscopy; GIM, gastric intestinal metaplasia; HP, *Helicobacter pylori*; NBI, narrow band imaging; Pro, prospective; Retro, retrospective; Sens, sensitivity; Spec, specificity; WLE, white light endoscopy; x, not reported.
* Years of experience of subgroups of endoscopists unknown.

Table 5. Current status of (the development of) AI systems per upper GI indication

Indications for AI in upper GI endoscopy	Current status of AI systems
BE neoplasia Detection, characterization, and delineation of BE neoplasia Selection of biopsy site	Algorithms are trained and validated with a dataset of labeled endoscopic images Prospective studies during live endoscopic procedures have been performed in small groups of patients Next step: Validation of AI algorithms in large groups of patients during live endoscopic procedures. Assess AI performance when used by endoscopists with different levels of experience
ESCC Detection of early ESCC Prediction of invasion depth	Algorithms are trained and validated with a dataset of labeled endoscopic images Retrospective studies with high quality images or videos haven been performed Next step: Prospective data collection of images and videos
EGC Detection of EGC Prediction of invasion depth	Algorithms are trained and validated with a dataset of labeled endoscopic images Retrospective studies with high quality images or videos Next step: Prospective data collection of images and videos
Gastric precancerous lesions GIM and HP infection CAG	Algorithms are trained and validated with a dataset of labeled endoscopic images Prospective data collection with high quality images Next step: Prospective studies during live endoscopic procedures

AI, artificial intelligence; BE, Barrett's esophagus; CAG, chronic atrophic gastritis; EGC, early gastric cancer; ESCC, esophageal squamous cell carcinoma; GI, gastrointestinal; GIM, gastric intestinal metaplasia; HP, *Helicobacter pylori.*

developed a CNN-CAD model for the detection of GIM with ME-NBI. The AI model reported a diagnostic accuracy of 89% with an accuracy of 84% for expert endoscopists with 10 years of endoscopic experience ($p = 0.42$).

Zheng et al. [67] developed a CAD system to determine HP infection status, based on endoscopic images. In total, 15,484 gastric images of 1,959 patients of which 1,157 with a HP infection were used. This study aimed to investigate whether the AI model could accurately diagnose HP infection during endoscopy without the need for biopsies. The CNN system showed a high performance with an accuracy of 92%. Nakashima et al. [69] used a DL model to diagnose HP infection with the use of WLE and blue light imaging (BLI). The research group conducted a single-center prospective study with 222 participants of which 105 had a confirmed HP infection. The DL model had an AUC of 0.96 with BLI. However, with WLE images, the AUC of the AI model decreased to 0.66.

Conclusion and Potential Challenges of Implementing AI Upper Endoscopy into Clinical Practice

In this review, we have shown that AI systems have been applied in upper GI endoscopy for several indications: (1) detection, characterization, and delineation of esophageal and GC and their premalignant conditions; (2) prediction of tumor invasion; and (3) diagnosis of a HP infection. The current status of AI models for each indication in upper GI endoscopy is shown in Table 5. So far, all AI studies in upper GI endoscopy have shown promising results with high performance for accurate detection and staging of (pre-)malignant lesions in both the esophagus and stomach. The benefit, especially on the quality of endoscopy by the use of AI in upper GI however, still needs to be demonstrated and may differ between endoscopists based on their skills and experience.

The use of AI in upper GI endoscopy may be of additional value for clinical practice for different reasons. AI has the potential to provide real-time assistance by red flagging cancers that remained undetected by endoscopists and may improve the yield of biopsies by indicating the optimal biopsy sites during live endoscopic procedures. More accurate prediction of tumor invasion of early-stage cancers may improve the selection of patients eligible for endoscopic resection and may prevent unnecessary invasive surgery. And more accurate endoscopic diagnosis of HP infection and gastric precancerous lesions by AI models may replace gastric biopsies.

To date, most AI models in upper GI endoscopy are developed in an ideal setting with high-quality imagery. This setting does not always reflect real-life endoscopy,

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where good visualization of the mucosa depends on the experience and skills of the endoscopists, which is essential for optimal performance of AI. Although several studies compared AI models to endoscopists, studies reporting on the diagnostic performance of AI models for each experience level of endoscopists are scarce. The outcome of these studies will better illuminate for which indication AI may be of additional value in relation to endoscopist's own experience and skills. For example, in GC, AI outperformed mid-level and trainee but not expert endoscopists. Besides studies linking the performance of AI models to endoscopists with different levels of experience, studies that investigate AI during real-time upper GI endoscopy are still very scarce. To date, no AI systems have been validated in large groups of patients during live endoscopic procedures. Large prospective trials are awaited for to validate the additional value and confirm the clinical significance of AI models during real-life endoscopy.

In conclusion, AI models in upper GI endoscopy showed high diagnostic performance for the detection, characterization, and delineation of upper GI lesions. In addition, AI shows promising results in the prediction of the tumor invasion depth and diagnosis of HP. The benefit of AI correlated to endoscopist skills and experience need to be further addressed, while prospective studies are needed to confirm its accuracy and feasibility during real-time daily endoscopy.

Conflict of Interest Statement

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M.C.V.S. was invited for this review and contributed to, with M.T., the conception and design; M.T. and L.T. jointly acted as first authors of this work, screened articles for inclusion in this review, interpreted data, and drafted the manuscript. A.D.K. co-authored the manuscript. All the authors critically edited, read, and approved the final manuscript.

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