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EDITORIAL

Opinion: How to manage subepithelial lesions of the upper gastrointestinal tract?

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Abstract

Subepithelial lesions (SELs) in the upper gastrointestinal (GI) tract are relatively frequent findings in patients undergoing an upper GI endoscopy. These tumors, which are located below the epithelium and out of reach of conventional biopsy forceps, may pose a diagnostic challenge for the gastroenterologist, especially when SELs are indeterminate after endoscopy and endoscopic ultrasound (EUS). The decision to proceed with further investigation should take into consideration the size, location in the GI tract, and EUS features of SELs. Gastrointestinal stromal tumor (GIST) is an example of an SEL that has a well-recognized malignant potential. Unfortunately, EUS is not able to absolutely differentiate GISTs from other benign hypoechoic lesions from the fourth layer, such as leiomyomas. Therefore, EUS-guided fine needle aspiration (EUS-FNA) is an important tool for correct diagnosis of SELs. However, small lesions (size < 2 cm) have a poor diagnostic yield with EUS-FNA. Moreover, studies with EUS-core biopsy needles did not report higher rates of histologic and diagnostic yields when compared with EUS-FNA. The limited diagnostic yield of EUS-FNA and EUS-core biopsies of SELs has led to the development of more invasive endoscopic techniques for tissue acquisition. There are initial studies showing good results for tissue biopsy or resection of SELs with endoscopic submucosal dissection, suck-ligate-unroof-biopsy, and submucosal tunneling endoscopic resection.

Key words: Gastrointestinal neoplasm; Gastrointestinal endoscopy; Endoscopic ultrasound-guided fine needle aspiration; Endosonography; Gastrointestinal stromal tumors

Core tip: Subepithelial lesions (SELs) of the upper gastrointestinal tract include a broader differential diagnosis, which can range from non-malignant tumors to lesions with malignant potential such as gastrointestinal stromal tumors. The possibility of having a potentially malignant lesion may bring anxiety and discomfort to patients and doctors. Further investigation should be carried out for patients with high-risk lesions after risk stratification. This editorial presents the current

evidence about the diagnostic management of SELs.

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TYPES AND DIAGNOSIS OF SUBEPITHELIAL LESIONS

Expansive lesions located below the epithelium of the gastrointestinal (GI) tract pose a diagnostic challenge for the gastroenterologist. In most cases, the endoscopic aspect is not diagnostic and lesions are out of reach for conventional biopsy forceps[1].

The differential diagnosis of subepithelial lesions (SELs) encompasses non-neoplastic lesions such as varices, as well as neoplastic lesions with practically no malignant potential, including leiomyoma or lipoma. However, there are neoplastic lesions with a higher malignancy potential, for example gastrointestinal stromal tumors (GISTs) and neuroendocrine tumors[2]. Dealing with patients with SELs is a real exercise in risk stratification.

In a few circumstances, the endoscopic aspect is sufficient to define a low risk lesion, such as a pancreatic rest located at the greater curvature of the antrum, or a large and ulcerated mass like a high grade gastric GIST. The challenge is the inconspicuous SEL clearly located below the mucosa[3].

Some endoscopic maneuvers should be employed to better characterize SELs: Chromoendoscopy and conventional biopsy are useful to rule out true mucosal neoplasms that rise deep in the epithelium, such as myoblastoma and neuroendocrine tumor. Measuring the lesion is also important. Changing patient decubitus and palpation with the biopsy forceps are usually employed to differentiate a true SEL from an extrinsic compression caused by other organs. Generally, these maneuvers have low sensitivity for defining the true nature of the lesions[4].

Sometimes it is relatively easy to make a differential diagnosis using endoscopic ultrasound (EUS), for example between a small gastric carcinoid limited to the deep mucosa and a compression of the GI tract caused by other extrinsic structures, such as a giant splenic cyst. However, in many circumstances the differential diagnosis is not straightforward, even with EUS. When we are dealing with intramural lesions, the EUS image will define the layer of the GI wall where the lesion lies.

Hypoechoic SELs from the fourth layer include a broader differential diagnosis, for example GIST, leiomyoma, and schwannoma, among other mesenchymal tumors.

RISK STRATIFICATION

Thinking about risk stratification, authors looked for some EUS features predictive of SEL malignancy. Larger, heterogeneous lesions with cystic areas and irregular outer margins were proved to harbor a higher risk for malignancy. The presence of at least two of these features had an 80% sensitivity and 80% specificity for detecting malignancy[4,5].

It is noteworthy that the location of the lesion can also predict its behavior. Esophageal SELs rarely harbor any malignant potential (1%), different from gastric and duodenal lesions which have a higher risk for malignancy, in more than 20% of cases[2].

Indeed, when SELs are located in the esophagus, the risk for a potential malignant lesion, such as a GIST, is low (7%). On the other hand, when the lesion is located in the stomach or duodenum this risk is much higher, as some publications reported that subepithelial neoplasms located in the stomach and duodenum were GISTs in more than 70% and 50% of cases, respectively[6,7].

When we looked at our experience[8], we also noticed that location inside the stomach could be useful for risk stratification. From 11 lesions located in the cardia, none were GISTs, while from 17 lesions located at the gastric body, 11 (70%) were GISTs.

Our numbers were confirmed in a larger trial[9], where 144 patients with SELs were endoscopically resected by endoscopic submucosal dissection (ESD). Only 14% of the lesions located at the cardia proved to be GISTs, while 85% were leiomyomas.

EUS is an important tool for the differential diagnosis of SELs. Its features can be diagnostic of extrinsic compressions, lipomas, cysts and varices, and no further investigation is needed.

GIST: ONCOGENESIS AND HISTOLOGIC ASSESSMENT

The concept of GISTs is relatively recent, and refers to a group of mesenchymal lesions that express a transmembrane protein called KIT. This KIT protein is codified by a proto-oncogene called c-kit. In normal conditions, the stem cell factor activates two kit receptors to signal cell proliferation, by activating tyrosine kinase. In GISTs pathogenesis, oncogenic mutations in KIT result in ligand-independent activation of tyrosine kinase. C-kit mutations located at exons 11 and 9 are the most frequent ones. Around 5% of GISTs do not present c-kit mutations; in those cases mutations of the platelet-derived growth factor are seen[10].

GISTs are rare tumors that affect patients in their fifties. In the United States, the estimated incidence of GIST is 7 to 14 new cases per million in the general population[11]. The most frequent locations of GISTs are the stomach and small bowel. The colorectum and esophagus are much less frequent locations, as well as the omentum, retroperitoneum and mesenterium[11].

Histologically, most GISTs are spindle cell type (70%). In the minority of cases, they present as epithelioid (20%) or mixed (10%) types[12]. It is controversial whether the histologic type has prognostic implications. The spindle cell type is practically identical to the histology of leiomyoma. Only an immunohistochemistry panel can make a differential diagnosis between them.

Immunohistochemistry testing at least for C-kit and CD34 is recommended. It is noteworthy that up to 40% of GISTs express smooth muscle actin[12].

GISTs have been included in the 2010 TNM classification, meaning that they should be regarded as malignant neoplasms. However, not all GISTs present invasive or metastatic behavior. Small bowel GISTs present a more invasive behavior when compared to gastric ones. The overall 5-year mortality rate for small bowel GISTs reaches up to 39%, compared to 17% for gastric GISTs[13,14]. Spindle cell GISTs have a higher 5-year disease-free survival rate[15], but these results have not been replicated. In addition, mutations at exon 11 are associated with a better response to target therapy, such as oral imatinib[16].

However, the most important factors that predict GIST behavior are size and mitotic rate[17]. In fact, these features are used for the 2010 TNM classification[18]. In that classification, gastric GISTs up to 2 cm with a low mitotic rate (< 5 mitoses per 50 high-power field), are staged as Ia.

CAN EUS DIFFERENCIATE GISTS FROM OTHER MESENCHYMAL TUMORS SUCH AS LEIOMYOMAS?

The answer is no. At least up to now.

Hunt *et al*[19] found that gastric hypoechoic lesions measuring more than 4 cm, with cystic spaces and ulceration, are probably GISTs. However, most of incidental SELs do not present these features.

Another publication[20] looked at the correlation between EUS and the final histology of small (< 2 cm) resected gastric SELs. It is noteworthy that none of the 22 patients had a GIST, probably because the authors did not resect lesions from the fourth layer, where GISTs usually lie. Most lesions were pancreatic rests, and the presumptive EUS diagnosis was correct in ten of the 22 cases, less than 50%.

In our experience using EUS[8], the presence of flow detected by power Doppler and irregular outer borders had a positive likelihood ratio of 10 for GIST diagnosis. But, from 21 patients with gastric GISTs, power Doppler was positive in only five cases (25%), and irregular outer borders in seven (35%). Therefore, the absence of these features does not rule out the diagnosis of GIST, or in other words, these features have a low negative predictive value for the diagnosis of GIST.

Recently, contrast-enhanced harmonic EUS (CEH-EUS) has been employed for differential diagnosis of gastric SELs. The results were positively convincing in the study by Kannengiesser *et al*[21], but with a limited cohort (fewer than 20 patients). CEH-EUS showed hyperenhancement of gastric lesions from the fourth layer that proved to be a GIST, and no enhancement of gastric leiomyoma.

Computed tomography (CT) and magnetic resonance imaging (MRI) may also be valid tools for GIST diagnosis, especially when a cytological diagnosis is unnecessary. In fact, a meta-analysis[22] that evaluated 4534 patients with GISTs, from 46 studies, showed that CT and MRI had a pooled diagnostic yield of 73% and 91% respectively.

CAN WE PREDICT GIST BEHAVIOR BY ENDOSCOPY OR EUS?

It has been observed that high grade GISTs double in size in 9 mo, while those with benign behavior do it in 18 mo.

Onishi *et al*[23] reported that hypoechoic spots were present in 84% of gastric GISTs which grew in size, and in 52% of gastric GISTs that remained stable in size (84.2% *vs* 51.9%, $P = 0.023$). Again, this is another interesting piece of information but useful only when it is present.

A previous study[24] looked at the use of CEH-EUS to predict GIST grade. Based on enhancement of features immediately after contrast administration (the vessel phase), and a few minutes after (the perfusion phase), gastric GISTs were classified as types Ⅰ and Ⅱ. All type Ⅰ lesions revealed low grade GISTs after resection. On the other hand, all type Ⅱ lesions were high grade GISTs. Once more, this is very interesting data that needs validation in a large cohort of patients.

TISSUE IS THE ISSUE

The bite-on-bite biopsy technique has been described for tissue acquisition of hypoechoic lesions of the fourth layer. However, some reports demonstrated low diagnostic yield of around 17%[25].

EUS-guided fine needle aspiration (EUS-FNA) is the logical procedure for tissue acquisition. A study by Hoda *et al*[26] performed EUS-FNA on gastric lesions with a mean size of 28 mm. They employed a standard 22 G needle, and the diagnostic yield was 62%.

When we remember that during EUS-FNA the GI wall, including the proper muscle layer, is sampled, the first question that comes to our minds is: Is EUS-FNA diagnosis correct? Apparently, the answer is yes. Stelow *et al*[6] reported, in a study of EUS-FNA with sufficient material from 29 patients with SELs and follow-up information, that EUS-FNA diagnosis was correct in 93% of patients, and in almost all cases of mesenchymal tumors.

EUS-FNA diagnosis of SELs may be correct, but the diagnostic yield is not so high for lesions smaller than 30 mm. EUS-FNA had an overall diagnostic yield of 40% to 50% for lesions measuring up to 10 mm, and of 60%

to 70% for lesions measuring from 11 to 30 mm[26]. In conclusion, EUS-FNA has a diagnostic yield of 60% to 70%, with a lower diagnostic yield for small lesions.

The next logical development would be to employ needles that make core biopsy possible. In a prospective study[27], the authors did not find any difference between EUS-FNA and EUS-trucut core biopsy of SELs. They employed the trucut biopsy needle model that was a rigid, 19 G needle. Needle malfunction was relatively common when the scope was in a bent position.

Now, there are new models of core biopsy needle available, such as the 19 G flexible nitinol needle, and the ingenious core trap, which come in different sizes. The first results with these new needles were presented a couple of years ago. In a limited cohort of patients, the diagnostic yield reached impressive figures.

Meta-analysis of 21 studies[28] comparing standard EUS-FNA and the ProCore needle for tissue acquisition of solid masses, including pancreatic masses, lymph nodes and SELs, showed no significant difference in the rates of diagnostic yield, diagnostic accuracy or histologic yield, between the two techniques.

Another meta-analysis[29] focused on diagnostic yield, and on the complication rate of EUS-FNA and EUS-guided core needle biopsy (EUS-CNB), for patients with GIST. The authors reached the same conclusion, *i.e.*, the diagnostic yield of EUS-FNA and EUS-CNB are the same, 65%. The EUS-FNA complication rate was 0.4%, and for EUS-CNB it was 1.1%. Death is rare but may occur after EUS-FNA of GIST, so one must beware of that.

Core biopsy is necessary for GIST diagnosis, and EUS-FNA provides core biopsy in 70% of cases, especially for lesions larger than 2 cm. EUS-core biopsy needles did not prove to be better; therefore, their higher cost is not justifiable. Severe complications and mortality are rare, but may occur after EUS-FNA and EUS-core needle biopsy of SELs.

ENDOSCOPIC TECHNIQUES FOR SEL DIAGNOSIS AND RESECTION

The limited diagnostic yield of EUS-FNA and EUS-core biopsy of SELs prompted the development of more aggressive endoscopic techniques for tissue acquisition. One of them [suck-ligate-unroof-biopsy (SLUB)] consists of placing an endoloop at the base of the lesion with the aid of a cap. After unroofing, biopsies are taken. A few months later, endoscopic and EUS control confirms the complete disappearance of the tumor. Not all fourth layer SELs can be treated by SLUB. The authors suggest that the dimension should not surpass 2 cm and, very importantly, the tumor should have no exophytic growth[30].

ESD is another option for tissue acquisition and treatment of SELs located at the cardia. In a large series[31] of 143 patients, the authors obtained a 95% complete resection rate of leiomyomas and GISTs, with a 4% perforation rate, and no recurrence in 2-year follow-up.

Submucosal tunneling endoscopic resection (STER)[32] involves the creation of a submucosal tunnel in the same fashion as the peroral endoscopic myotomy procedure. The tumor is then resected, and the mucosal incision site is closed, which guarantees the safety of the procedure, even in cases of perforation.

The first published series[32] includes fewer than 20 patients. The majority of them had SELs in the esophagus and cardia. In this paper, only three cases with gastric lesions were treated by STER. It should be remembered that most esophageal SELs are benign leiomyomas.

A word of caution is advised for those interested in these innovative procedures such as SLUB and STER. EUS is absolutely necessary to select lesions suitable for these techniques. In this scenario, a CT scan often demonstrates a smooth outer contour of gastric SELs. However, in the operative field, it is clear that the lesion may project to the serosal surface, making SLUB and STER very dangerous.

CONCLUSION

In conclusion, SELs that are indeterminate after endoscopy and EUS examinations may have a challenging diagnosis. Otherwise, as mentioned before, if the aspect is typical of a neuroendocrine tumor, a pancreatic rest, lipoma, cyst, or varices, management poses no major problems. If EUS demonstrates small hypoechoic tumors of the second and third layers, endoscopic resection is possible and quite safe. For small hyperechoic lesions of the second and third layers, endoscopic resection is a valid alternative. For larger lesions, a tissue diagnosis is necessary. For larger lesions of the fourth hypoechoic layer, EUS-FNA and core biopsy are safe and have a good diagnostic yield. Some authors advocate referring the patient directly for surgery, if the lesion is located in the stomach or in the duodenum. SLUB, STER, and ESD are techniques under investigation for SELs.

Small hypoechoic lesions of the fourth layer should be simply followed (every six months for one year, and then yearly or biannually), especially if EUS features indicate a benign lesion. Oh the other hand, if EUS features are worrisome, EUS-FNA or core biopsy should be tried, but they have a very low diagnostic yield in small lesions. Surgery is a reasonable option especially if the lesion is located in the stomach or duodenum. Again, ESD, SLUB, and STER are under investigation.

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Advanced endoscopic imaging of indeterminate biliary strictures

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Abstract

Endoscopic evaluation of indeterminate biliary strictures (IDBSs) has evolved considerably since the development of flexible fiberoptic endoscopes over 50 years ago. Endoscopic retrograde cholangiography pancreatography (ERCP) was introduced nearly a decade later and has since become the mainstay of therapy for relieving obstruction of the biliary tract. However, longstanding methods of ERCP-guided tissue acquisition (*i.e.*, biliary brushings for cytology and intraductal forceps biopsy for histology) have demonstrated disappointing performance characteristics in distinguishing malignant from benign etiologies of IDBSs. The limitations of these methods have thus helped drive the search for novel techniques to enhance the evaluation of IDBSs and thereby improve diagnosis and clinical care. These modalities include, but are not limited to, endoscopic ultrasound, intraductal ultrasound, cholangioscopy, confocal endomicroscopy, and optical coherence tomography. In this review, we discuss established and emerging options in the evaluation of IDBSs.

Key words: Cholangiocarcinoma; Bile duct diseases; Cholangiopathies; Gastrointestinal endoscopy; Pancreatic adenocarcinoma

Core tip: Indeterminate biliary strictures (IDBSs) remain a considerable challenge for endoscopists, clinicians, surgeons, and other medical professionals as well as patients. The limitations of current technologies have helped drive the search for novel techniques aimed to enhance the evaluation of IDBSs and thus improve diagnosis and clinical care. Here we review existing and emerging techniques and provide a synopsis of current understanding of their strengths, limitations, and role in the evaluation of IDBSs.

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INTRODUCTION

A substantial proportion of biliary strictures cannot be classified as benign or malignant on the basis of non-invasive imaging, endoscopic retrograde cholangiopancreatography (ERCP), and/or routine tissue sampling methods (*i.e.,* biliary brushing, intraductal forceps biopsy)[1]. Although the addition of fluorescence *in situ* hybridization (FISH) to conventional biliary cytology has been useful in assessing strictures with a higher suspicion for malignancy which may benefit from closer follow-up, sensitivity remains low. As a result, these "indeterminate biliary strictures" (IDBSs) remain a clinical challenge, especially when considering the resulting delayed diagnosis, deferred implementation of care, economic impact from repeated evaluations, and resulting angst among patients, clinicians, and endoscopists.

IDBSs may arise *de novo* or in patients with known chronic biliary disease. They typically manifest with (abrupt onset or slowly progressive) jaundice, pruritus, right upper quadrant pain, and/or cholangitis. IDBSs may also be incidentally discovered, often following abdominal computed tomography or magnetic resonance imaging performed for other indications. The differential diagnosis of IDBSs is broad (Table 1), and determination of the underlying etiology and pathobiology is often challenging. Endoscopic evaluation of IDBSs has traditionally consisted of ERCP, but several other ancillary techniques have been developed to help address this common diagnostic challenge.

In this article, we review these ancillary techniques, providing our current understanding of their strengths, limitations, and role in the evaluation of IDBSs.

ERCP

ERCP provides fluoroscopic images of the biliary tree and provides the primary portal for diagnosis and intervention. Cholangiographic features suggestive of a malignant stricture include length (> 14 mm), irregularity, abrupt shelf-like borders, presence of intraductal polypoid or nodular areas, and the presence of simultaneous common bile duct (CBD) and pancreatic duct dilation (*i.e.,* double duct sign)[2,3]. Efforts to improve the sensitivity of cholangiography have led to methods for tissue acquisition; however, conventional methods such as biliary brush cytology, intraductal biopsy, and fine needle aspiration (FNA) have yielded disappointingly low sensitivity for detecting malignancy. For example, a recent review of the literature that identified 16 studies reported an overall biliary brush cytology sensitivity of 42% with a negative predictive value (NPV) of 58%[4]. The poor sensitivity was attributed to sampling error, inadequate specimen (*e.g.,* due to desmoplastic reaction or biliary fibrosis), and/or difficult cytopathologic distinction of subtle differences between malignant and nonmalignant cells[5,6]. Biliary cytopathology interpretation is often challenging, even within high-volume centers. A recent meta-analysis by Navaneethan *et al*[7] compared the effectiveness of brush cytology and intraductal biopsy for evaluating biliary strictures; nine studies were included, and the pooled sensitivity and specificity for brushings was 45% and 99%, respectively, compared to 48% and 99% for intraductal biopsies, respectively. When the two modalities were combined, there was some incremental yield, with sensitivity improving to 59%[7]. Methods tested to potentially further increase the diagnostic sensitivity have included use of longer brush length, initial stricture dilation, and repeated brushing, with repeat brushing appearing to be most effective, albeit still with suboptimal results[8,9]. Intraductal FNA has also been associated with disappointing results, as data from five series (220 patients) demonstrated a sensitivity of 34%, in part perhaps due to technical challenges with performing intraductal FNA[10]. The suboptimal diagnostic performance of conventional tissue sampling techniques has provided the impetus for developing advanced cytologic methods such as FISH, digital image analysis (DIA), and flow cytometry, which are described further in a subsequent section.

A "dominant stricture" is a subtype of IDBS that arises in the setting of underlying primary sclerosing cholangitis (PSC) or other fibrosing cholangiopathies and may be loosely defined as a CBD stenosis of $\leqslant$ 1.5 mm or hepatic duct stenosis $\leqslant$ 1 mm in diameter[11]. Accurately detecting malignancy in the setting of PSC is especially critical given the 1560-fold increased risk of developing cholangiocarcinoma (CCA) in this cohort compared to the general population[12]. However, this imposes an even greater diagnostic challenge, as ERCP-guided approaches to tissue acquisition have performed poorly in this disease, with sensitivity ranging from 18%-40%[11,13,14]. Reasons for low sensitivity include but are not limited to periductal (or submucosal) as opposed to radial growth of some CCAs, desmoplastic reaction, and inadequate access of endoscopic devices and sampling under indirect visualization (chiefly due to the stenotic nature of the disease)[15]. Adjunctive modalities for endoscopic evaluation of IDBSs in this high-risk subset of patients may provide improved diagnostic value and are discussed below in their respective sections.

ADVANCED CYTOLOGIC TECHNIQUES FOR ERCP-ACQUIRED BILIARY BRUSHING SPECIMENS

Fluorescence in situ hybridization

FISH is a cytogenic technique that employs fluorescently labeled DNA probes to chromosomal loci of interest

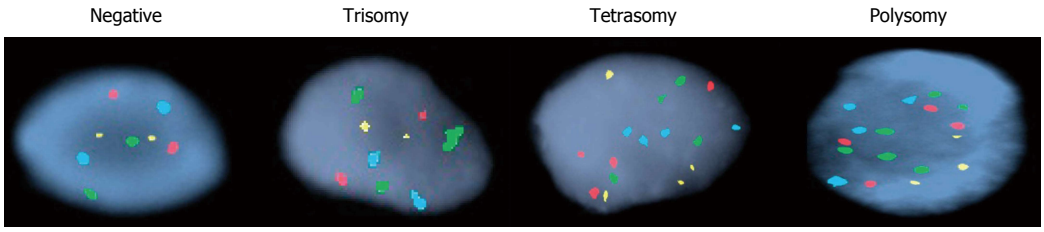

Figure 1 Representative fluorescence *in situ* hybridization microscopic image. Shown above are individual cells from biliary brushings showing distinct fluorescence *in situ* hybridization (FISH) results (arranged from lowest to highest risk of malignancy) using centromere enumeration probes (CEPs) to chromosomes 3 (red), 7 (green), 17 (aqua) and the 9p21 locus (gold). Potential FISH results include negative (two copies of each probe), trisomy 7 (≥ 10 cells with ≥ 3 CEP 7 signals and ≤ 2 signals for the other probes), tetrasomy (≥ 10 cells with four signals for all four probes), and polysomy (≥ 5 cells with ≥ 3 signals for ≥ 2 of the four probes).

Table 1 Potential etiologies of indeterminate biliary stricture

Benign
Primary sclerosing cholangitis
IgG4-associated cholangiopathy
Postoperative stricture (anastomotic, ischemic, cholecystectomy-related)
Ischemia (*e.g.*, hepatic artery thrombosis)
Infections (HIV cholangiopathy, parasites)
Pancreatitis (acute, chronic, autoimmune)
Choledocholithiasis
Mirizzi syndrome
Eosinophilic cholangitis
Vasculitis
Radiation
Portal biliopathy
Malignant
Pancreatic adenocarcinoma
Cholangiocarcinoma
Hepatocellular carcinoma
Lymphoma
Metastatic adenocarcinoma (*e.g.*, compressive lymphadenopathy)

HIV: Human immunodeficiency virus.

and thereby reveals losses or gains in these specific loci (*i.e.,* aneuploidy). Fluorescence microscopy is then used to quantify cells containing nuclei with abnormal probe signal numbers (Figure 1). The presence of ≥ 5 such cells showing gains of ≥ 2 of the (currently four) probes on FISH analysis, *i.e.,* polysomy, has been found to provide improved sensitivity compared to cytology while maintaining comparable specificity[16-20]. Recent studies have reported that incorporating 9p21 (*i.e.,* CDKN2A locus, critical in cell cycle progression and senescence[21,22]) deletion into the diagnostic criteria further improves the sensitivity to 76%-89%[23,24]. In individuals with PSC, detection of polysomy during subsequent ERCPs (*i.e.,* serial polysomy) or detection of polysomy in multiple segments of the biliary tree (*i.e.,* multifocal polysomy) appears to denote even greater risk of CCA[25,26].

DIA

DIA incorporates digital conversion and computer analysis to quantify nuclear DNA content and evaluate nuclear features; when compared to conventional cytology, it has been shown to have a higher sensitivity (39% *vs* 18%) but at the expense of lower specificity (77% *vs* 98%)[27]. In two studies comparing DIA with FISH, DIA appeared to have slightly lower sensitivity (38%-43% *vs* 44%-45%) and specificity (92%-95% *vs* 98%-100%). In one of the studies, routine cytology had a sensitivity of 15% and specificity of 100%, whereas in the other, DIA and FISH were performed only after negative cytology and histology[16,18]. Moreover, multivariable analysis of advanced cytologic methods in the evaluation of IDBSs showed FISH polysomy to be an independent predictor of malignancy, whereas DIA was not[19]. Despite the somewhat enhanced diagnostic sensitivity, the associated decrement in specificity has eliminated the use of DIA in many centers.

Flow cytometry

Flow cytometry relies on the detection of hyperploidy to identify malignant cells; it has similar sensitivity to routine cytology (42%) but has inferior specificity (77% *vs* 92%)[28]. It is not routinely used in the clinical evaluation of IDBSs.

ENDOSCOPIC ULTRASOUND

Endoscopic ultrasound (EUS) is increasingly being utilized in the evaluation of biliary strictures since reports of its first application in the mid-1980s[29,30]. Most of the hepatobiliary system can be examined with curvilinear echoendoscopy (EUS) from the gastric antrum (for visualization of the gallbladder), duodenal bulb (for visualization of the mid-CBD up to the confluence of the left and right hepatic ducts), or second portion of the duodenum (for visualization of the periampullary region)[31,32]. In addition, EUS provides other key information, including lymph node (Figure 2A), portal vein, and hepatic artery status for staging and through the detection of malignant ascites, omental deposits, and hepatic metastasis. Furthermore, EUS-guided FNA (Figure 2B) offers a minimally-invasive means for diagnostic tissue sampling (Table 2).

EUS with or without FNA may be useful in distinguishing malignant from benign biliary strictures. EUS findings of a pancreatic head mass (causing a biliary stricture secondary to extrinsic compression), an irregular outer edge of the bile duct wall, or bile duct wall thickness > 3 mm have been associated with malignancy when

Table 2 Comparison of advanced endoscopic imaging modalities

	Advantages	Disadvantages
ERCP	Widely available	Procedural risks
	Workhorse technique with numerous accessories	Fluoroscopic (and endoscopic) images only
	Facilitates other diagnostic modalities (*e.g.*, biliary brushing, biopsy, endomicroscopy) as well as therapy	Low sensitivity of conventional cytology and intraductal biopsies
EUS	Provides staging information	Limited views of the intrahepatic biliary tree (and non-visualization of the right intrahepatic ductal system)
	Permits FNA	Generally nondiagnostic in and of itself without FNA
	Can facilitate difficult biliary cannulation	Risk of tumor seeding if FNA primary tumor
IDUS	Can help direct ERCP-guided tissue acquisition	Limited depth of imaging
		Infrequently used in routine practice
Cholangioscopy	Excellent visualization of the biliary mucosa (with digital cholangioscopes)	High cost (disposable system $2000 per case)
	May improve sensitivity, specificity, and overall accuracy compared to ERCP alone	Likely higher rates of pancreatitis, cholangitis, and perforation compared to ERCP alone
		Time-consuming
		Not widely available
CLE	Excellent sensitivity and negative predictive value	Marginal interobserver agreement
	Provides imaging at a cellular and sub-cellular level (lateral resolution of 3.5 μm)	Contact imaging of a very limited regional surface
		Time-consuming
		Not widely available
OCT	High resolution	Suboptimal sensitivity
	Improved sensitivity compared to ERCP-guided tissue acquisition	Resolution not as high as CLE
	Highly specific	Not widely available
	Permits larger surfaces areas to be examined compared to CLE	Not well-validated

ERCP: Endoscopic retrograde cholangiopancreatography; EUS: Endoscopic ultrasound; IDUS: Intraductal ultrasound; CLE: Confocal laser endomicroscopy; OCT: Optical coherence tomography; FNA: Fine needle aspiration.

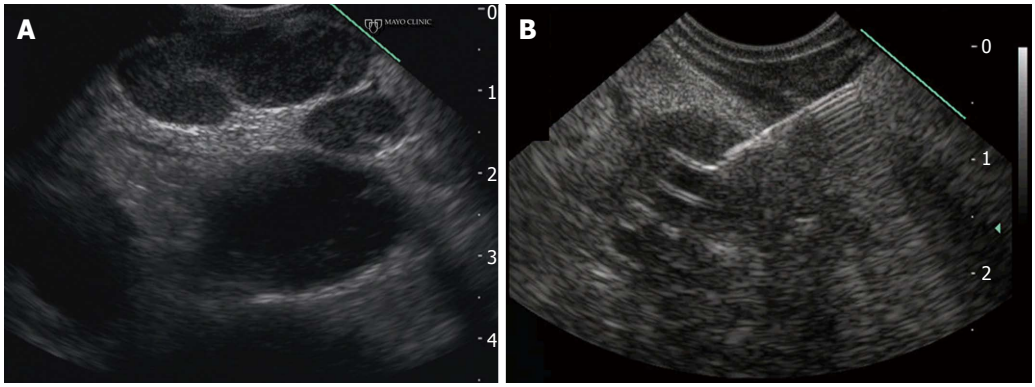

Figure 2 Endoscopic ultrasonographic findings in a patient found to have locally-advanced cholangiocarcinoma. A: Malignant lymphadenopathy; B: Endoscopic ultrasound-guided fine needle aspiration of primary cholangiocarcinoma.

evaluating IDBSs[33]. In a meta-analysis of nine studies including 555 patients, EUS without FNA was found to diagnose a malignant biliary stricture with a sensitivity and specificity of 78% and 84%, respectively[34]. The addition of FNA provides even more encouraging results, as a separate meta-analysis of 9 studies including 284 patients undergoing EUS-FNA demonstrated a sensitivity and specificity of 84% and 100%, respectively[35]. Many of these studies were performed following unsuccessful ERCP diagnosis, thus suggesting the value of EUS-FNA even among this more difficult-to-diagnose cohort.

A factor that appears to influence the sensitivity of EUS-FNA is the location of the stricture: Proximal (intrahepatic or hilar) *vs* distal (extrahepatic). In one study, the sensitivity for distal CCA was significantly higher than that for proximal CCA (81% *vs* 59%)[36]. This is perhaps explained by the greater ease of imaging and sampling of distal lesions as compared to proximal, which may be an important consideration when comparing EUS-FNA to ERCP data. Rösch *et al*[37] found EUS-FNA to be inferior to ERCP in patients with hilar biliary tumors (25% *vs* 75%) but superior for distal malignant strictures (60% *vs* 38%). Another variable that may impact performance of EUS-FNA is the presence of a bile duct stent, which results in acoustic shadowing and may occasionally interfere with sonographic imaging and FNA[38]. However, published data have not found the presence of plastic bile duct stents to lower the yield of EUS-FNA in the evaluation of IDBSs or suspected CCA[39].

A major limitation of EUS-FNA remains the concern for potential seeding of malignant cells along the needle track. This is less problematic for pancreatic head

lesions, as the path of trans-duodenal sampling would be resected during potential subsequent pancreatoduodenectomy. The concern is predominantly for proximal bile duct lesions, which require traversal of the hepatoduodenal ligament portion of the lesser omentum, which may not be resected during potential subsequent surgical intervention. In a series of 191 patients with hilar CCA receiving neoadjuvant chemoradiation followed by liver transplantation, 16 underwent transperitoneal FNA, and of the 6 (38%) that were positive for malignancy, 5 (86%) were later found to have peritoneal metastasis at operative staging *vs* 14/175 (8%) who did not undergo transperitoneal biopsy ($P < 0.01$)[40]. While nearly all patients in this study underwent FNA *via* a percutaneous route, the same concerns exists for EUS-guided FNA. Due to the potential for needle tract seeding, EUS-FNA of a primary bile duct tumor is considered a contraindication to liver transplantation; however, a recent retrospective study showed that preoperative EUS-FNA in patients with CCA did not affect overall or progression-free survival[41]. Until additional studies have further explored this area of uncertainty, biliary specimens to rule out CCA should be acquired intraductally rather than transmurally (*e.g.,* percutaneous or trans-duodenal) if liver transplantation is a consideration.

INTRADUCTAL ULTRASOUND

Intraductal ultrasound (IDUS) employs a thin (2.0-3.1 mm), high frequency (12-30 MHz) wire-guided radial ultrasound probe that is passed through the working channel of a duodenoscope and into the pancreatobiliary system during ERCP. With a radial penetration of 2 cm, IDUS allows for high-resolution characterization of IDBSs. Two to three mural layers are visualized during IDUS: (1) an inner hypoechoic layer representing mucosa, muscularis propria, and the fibrous layer of serosa; (2) an outer hyperechoic layer representing subserosal adipose tissue and serosa; and (3) sometimes an interface layer between bile and the inner hypoechoic layer[42].

IDUS features that have been associated with malignant rather than benign biliary strictures include sonographic disruption of the choledochal wall layers, wall thickening or irregularity, a hypoechoic mass with irregular margins, sessile tumor, infiltration of adjacent tissue or vasculature, or the presence of enlarged lymph nodes[43-45].

The published literature suggests that IDUS, although not often used in routine clinical practice, can be a useful ancillary technique in the evaluation of IDBSs. A retrospective review by Meister *et al*[46] of patients undergoing ERCP with IDUS demonstrated sensitivity as well as specificity of 98%, and a meta-analysis of 5 other studies found that IDUS accuracy for malignancy ranged from 84%-95%. Studies have also demonstrated that adding IDUS to ERCP-guided tissue acquisition improved sensitivity from 41%-68% to 90%-93%[47-49]. Domagk *et al*[50] found a combination of ERCP and IDUS to correctly diagnose malignancy in 88% of patients *vs* 76% and 58% of patients by ERCP alone and MRCP, respectively. Compared to EUS, IDUS has been shown to have greater sensitivity (91% *vs* 76%) and accuracy (89% *vs* 76%) in differentiating a malignant from a benign stricture[51]. IDUS was also found to have superior sensitivity (88% *vs* 63%) and specificity (91% *vs* 53%) in patients with PSC compared to ERCP alone[52].

IDUS, in a single experience reported cancer staging of T1, T2, T3/T4, N0 and N1 to be 84%, 73%, 71%, 69% and 69% accurate, respectively[46]. These results are intriguing; the low accuracy with N staging may be attributable to the limited depth of ultrasonic penetration, which limits IDUS largely to characterizing the mural features of the IDBS[51].

CHOLANGIOSCOPY

Cholangioscopy involves the use of a small-caliber, flexible endoscope to directly inspect the biliary epithelium and facilitate targeted sampling. The cholangioscope (daughter scope) is typically passed either through the working channel of a therapeutic (mother) scope during ERCP (Figure 3) or *via* direct peroral cholangioscopy following endoscopic papillotomy and percutaneous transhepatic cholangioscopy. Early cholangioscopy typically required two skilled endoscopists; this has since evolved to a single endoscopist effort with as-needed nurse assistance. In the last decade, a single-operator cholangioscopy system (SpyGlass Direct Visualization System, Boston Scientific Endoscopy, Marlboro, MA) with capability for 4-way tip deflection, a channel for insertion of a reusable fiberoptic probe, and irrigation and working channels, has been introduced. This system was severely hampered by poor image quality, but recent modifications, including the use of a video chip, has markedly improved image quality. Other cholangioscope options also exist, as alluded to above, but are currently not utilized clinically in the United States[53,54].

Cholangioscopy can help distinguish malignant from benign strictures, particularly *via* examination of epithelial vascular pattern (*e.g.,* irregularly dilated tortuous vessels, *i.e.,* "tumor vessels"), which is 100% specific and 96% sensitive when combined with targeted biopsies[55,56]. The presence of nodules, ulceration, or papillary or villous mucosal projections also suggest malignancy and warrant targeted biopsies[57].

Studies examining direct peroral or percutaneous cholangioscopy with or without biliary mucosal biopsies have demonstrated a sensitivity of 77%-100% and specificity of 79%-100%, with tissue adequacy achieved in 82%-97% of patients[58-63]. Addition of cholangioscopy to ERCP-guided tissue sampling enhances sensitivity for the diagnosis of biliary malignancy. For example, Fukuda *et al*[58] reported the sensitivity and accuracy of ERCP guided cytology and/or forceps biopsy improved from 58% and 78% to 100% and 93%, respectively. In a study by Draganov *et al*[63], sensitivity and accuracy of cytology, forceps biopsy, and cholangioscopy-guided mini-

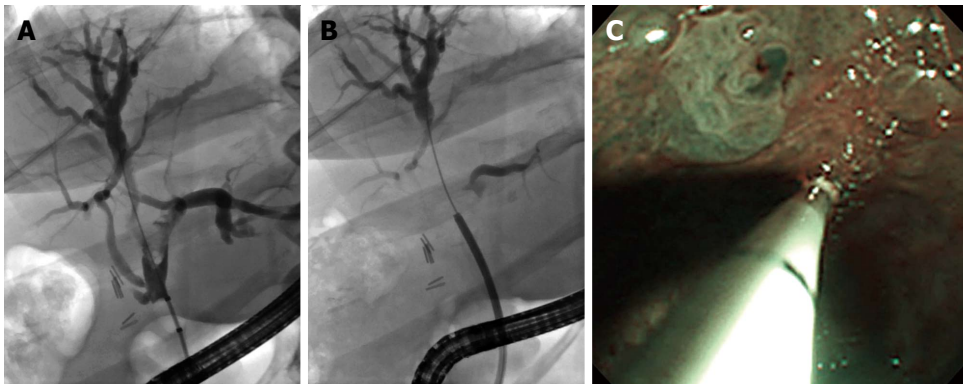

Figure 3 Passage of a SypGlass digital cholangioscope through a therapeutic duodenoscope to better evaluate hilar strictures and filling defects. A: Hilar (primarily right anterior hepatic duct) stricture and filling defects seen during endoscopic retrograde cholangiography pancreatography; B: SypGlass cholangioscope being passed through the working channel of therapeutic duodenoscope to better assess biliary stricturing and filling defects; C: SpyGlass cholangioscopy with narrow band imaging revealing villiform biliary mucosal changes; targeted biopsies were obtained and revealed low grade dysplasia concerning for early cholangiocarcinoma.

forceps biopsy were as follows: 5.8% and 39%, 29% and 54%, and 77% and 85%, respectively; mini-forceps biopsy was significantly more sensitive and accurate than cytology (P = 0.0001) or forceps biopsy (P = 0.0215) alone. Chen *et al*[64] reported the sensitivity and specificity of ERCP, cholangioscopy, and cholangioscopy-directed tissue biopsies to be 51% and 54%, 78% and 82%, and 49% and 98%, respectively, thus demonstrating much greater sensitivity and specificity for cholangioscopy with or without biopsy compared to ERCP alone.

The benefit of cholangioscopy over ERCP in patients with PSC and for distinguishing malignant from benign dominant strictures has also been demonstrated. In a study of 53 patients with PSC and dominant stricture, Tischendorf *et al*[52] used cholangioscopic findings of a polypoid or villous mass or irregularly shaped ulcer to classify malignancy before confirmation with standard tissue acquisition. This cholangioscopic finding provided greater sensitivity (92% *vs* 66%) and specificity (93% *vs* 51%) with a better NPV (97% *vs* 84%) than ERCP alone[52]. Cholangioscopy in the setting of PSC is often severely hampered by the number and severity of biliary stenosis. Cholangioscopy is performed predominantly under water immersion; alternatively, carbon dioxide gas insufflation can be used (predominantly during direct peroral cholangioscopy) and provides a distinctly different appearance to the biliary mucosa. Differences between the two imaging approaches may have individual value, *e.g.,* interpreting subtle surface mucosal change *vs* mucosal surface vascular pattern changes.

Video chip-based cholangioscopes are also equipped with narrow band imaging (NBI) (Figure 3C). NBI is based on the observation that the depth of light penetration depends on wavelength; the longer the wavelength, the deeper the penetration. Standard color video chips provide images based on sequential red-green- and blue illumination. The image is passed directly through selective band filters which highlight the red and blue bands. Blue light penetrates only superficially, whereas red light penetrates into deeper layers. The selective color imaging enhancement highlights mucosal surface detail and more so, mucosal vascular patterns[65-67]. An initial feasibility study involving 21 patients with biliary lesions found visualization of 57% of lesions to be "excellent" using NBI *vs* 9.5% using conventional white-light imaging[68]. A recent, small series of patients with PSC also led to the conclusion that NBI allowed better determination of tumor margins and increased detection of suspicious lesions compared to white-light imaging; the authors could not demonstrate an improved dysplasia detection rate, but this may have been consequent to methodological issues[69].

Relatively few studies have compared the diagnostic yield of cholangioscopy *vs* EUS. In one retrospective series of 66 patients undergoing evaluation of IDBSs with cholangioscopy combined with EUS, sensitivity and specificity for combined modalities was greater than for either modality alone[70]. In another study, 39 patients with negative brush cytology underwent EUS-FNA first and only proceeded to cholangioscopy if EUS was negative; EUS-FNA was diagnostic in 23 patients (58%), and the remainder of the patients required cholangioscopy, thus leading the authors to conclude that cholangioscopy could be reserved for cases where EUS-FNA is nondiagnostic[71].

Potential adverse events of cholangioscopy include pancreatitis, cholangitis, perforation, hemobilia, and sphincterotomy bleeding. A recent retrospective study found that patients undergoing ERCP with cholangioscopy had significantly higher rates of pancreatitis (2.2% *vs* 1.3%), cholangitis (1.0% *vs* 0.2%), and perforation (1.0% *vs* 0.3%) than ERCP alone[72]. However, multivariable analysis did not find cholangioscopy to be associated with an increased rate of adverse events compared to ERCP[73].

CONFOCAL LASER ENDOMICROSCOPY

Confocal laser endomicroscopy (CLE) is an emerging imaging modality that permits high-resolution, *in vivo* assessment of the biliary epithelium. It provides real-time contact imaging at a cellular and sub-cellular

level, offering a lateral resolution of 3.5 μm, optical slice thickness of 30 μm, and optical penetration of 40-70 μm. CLE is based upon the principle of illuminating a tissue with a low-power laser and then detecting reflected fluorescent light. The laser is focused at a specific depth, and only light which is reflected back from that plane is refocused and able to pass through the pinhole confocal aperture; the term "confocal" hence refers to the fact that the reflected light is refocused onto the detection system by the same lens through which the laser light was initially emitted. As a result, scattered light from above and below the plane of interest is not detected, thereby increasing spatial resolution. A focused, scanning light source (*i.e.,* laser) and processor then generate reconstructed grayscale images of the target area, enabling epithelial and subepithelial visualization. Notably, CLE requires administration of intravenous or topical contrast (typically fluorescein) to highlight tissue features and better differentiate normal architecture or inflammatory changes from neoplastic tissue.

A CLE imaging probe (pCLE) can be passed through various ERCP catheters or through the working channel of a cholangioscope. In the first study of pCLE for the evaluation of IDBSs, Meining *et al*[74] reported that the visualization of irregular, dilated ("angiogenic") vessels predicted malignancy with a sensitivity of 83% (compared to 50% for standard histopathology), specificity of 88%, and accuracy of 86% among 14 patients. A subsequent study with 37 patients revealed similar findings[75]. In an effort to more uniformly identify pCLE imaging findings associated with malignancy, a standardized classification system (*i.e.,* Miami classification) was proposed consisting of: (1) the presence of thick, white bands (> 20 pm); (2) thick dark bands (> 40 μm); (3) dark clumps; (4) epithelial structures; and (5) fluorescein leakage[76]. Suggested criteria for benign strictures were: (1) thin, dark (branching) bands; and (2) thin, white bands. In a blinded consensus review that validated this classification schema, combining two or more of the criteria suggestive for malignancy (except fluorescein leakage) provided a sensitivity, specificity, positive predictive value (PPV), and NPV of 97%, 33%, 80%, and 80%, respectively, compared with 48%, 100%, 100%, and 41% for standard tissue acquisition[77]. Interobserver variability was moderate for most of the criteria. A prospective, multicenter study assessing the role of pCLE in the evaluation of 89 patients with IDBSs reported a sensitivity, specificity, PPV, and NPV of 98%, 67%, 71%, and 97% for the detection of malignancy, respectively, compared with 45%, 100%, 100%, and 69% for index pathology[78]. Moreover, when combined with ERCP, pCLE was significantly more accurate than ERCP with tissue acquisition (90% *vs* 73%). Among the subset of patients with PSC, a small retrospective study found that pCLE detected malignancy with a sensitivity, specificity, PPV, and NPV of 100%, 61%, 22.2% and 100%, respectively, compared to 0%, 94.4%, 0% and 89% with standard tissue sampling[79]. Given its high sensitivity and NPV, pCLE may ideally be used to exclude malignancy in this high-risk population. The technique is limited by the need for point contact and by movement. Additional study is needed to optimize image interpretation and to determine the cost benefit.

A limitation of the Miami classification is the suboptimal interobserver agreement. In contrast to the initially reported moderate interobserver variability with most criteria, a subsequent study among 6 experienced endoscopists from 5 institutions reviewed 25 de-identified pCLE video clips of IDBSs and found interobserver agreement for individual criteria to range from poor to fair and for final diagnosis to be slight[80]. Further training and standardization is needed to improve interobserver reliability, as may be expected with most evolving techniques[81].

In an effort to improve the low specificity of pCLE, which has been attributed to inflammatory changes (*e.g.,* chronic inflammation, stent-related changes, previous endoscopic procedures), descriptive criteria (*i.e.,* Paris classification) have recently been proposed[82]. These criteria aim to distinguish benign inflammatory strictures by assessing for vascular congestion, dark glandular patterns, increased interglandular space, and thickened reticular structures, and reportedly have increased the specificity from 64% to 76%[82]. A prospective, multicenter study evaluating 112 patients with IDBSs incorporating the Paris classification found pCLE to be 89% sensitive, 71% specific, and 82% accurate compared with 56%, 100% and 72% with standard tissue sampling alone[83].

OPTICAL COHERENCE TOMOGRAPHY

Optical coherence tomography (OCT) is analogous to ultrasound but relies on low-intensity infrared light (700 to 1500 nm wavelength range) instead of sound to generate high-resolution, cross-sectional tissue imaging. The delay in time of light back-scattered by the various tissues is measured using a technique known as low coherence interferometry, which has a depth of penetration of 1-3 mm and lateral and axial resolution down to 10 μm. This technology provides much greater spatial resolution than IDUS and, unlike endomicroscopy, does not require contrast administration. OCT achieves visualization of layer architecture similar to histologic sections[84,85]. In doing so, OCT allows visualization of microscopic structures such as blood vessels, lymphoid aggregates, crypts, and submucosal glands and can aid in differentiating malignant from benign tissue in real-time[86-88]. Miniaturization of early OCT probes has enabled insertion into a transparent biliary catheter that can be passed through the working channel of an ERCP scope for biliary cannulation and *in vivo* imaging[89].

OCT has been shown to increase the sensitivity for detecting malignant biliary strictures as compared to biliary brushing cytology alone. Arvanitakis *et al*[90] evaluated 2 OCT criteria, namely unrecognizable layer architecture and presence of large nonreflective areas compatible with tumor vessels, for diagnosing malignant

strictures when compared to the gold standard of tissue acquisition in 35 patients undergoing ERCP for evaluation of IDBSs. Nineteen patients ultimately had malignant strictures, and these 2 OCT criteria were associated with a sensitivity, specificity, PPV, NPV and accuracy of 53%, 100%, 100%, 64% and 74%, respectively. The sensitivity of biliary mucosal brushings and/or biopsy improved from 67% to 84% when at least 1 criterion was added. In another study, the diagnostic utilities of OCT and ERCP-guided brush cytology were compared while evaluating 12 patients with main pancreatic duct stricture. Six patients ultimately had malignancy and OCT demonstrated greater sensitivity (100% *vs* 67%) than cytology while maintaining equal specificity (100%)[91]. OCT, unlike confocal imaging, permits larger surfaces areas to be examined. Improved resolution is paramount. The limited existing data are encouraging, but additional studies are awaited to better define the potential role of OCT in evaluating IBDSs, particularly among patients with high-risk conditions such as PSC.

FUTURE DIRECTIONS

Other technologies may be amenable to use in the evaluation of IDBSs. These include high-resolution endomicroscopy, Raman spectroscopy, EUS elastography, and CLE with chromocholangioscopy or autofluorescence. Each will be challenged by the need for miniaturization and must satisfy value in the face of added cost.

CONCLUSION

IDBSs pose a diagnostic challenge for which more accurate diagnostic tests are critically needed. Although ERCP offers therapeutic options for biliary obstruction, conventional methods of tissue acquisition remain generally insensitive, albeit to a lesser degree with use of advanced cytologic techniques such as FISH. EUS can be of additional benefit in evaluating distal strictures and staging, though concerns remain regarding tumor seeding. IDUS may supplement ERCP and EUS and aid in local staging but, despite its longstanding availability, is seldom employed. Cholangioscopy permits direct visualization and directed sampling; design enhancements may simplify its use and improve performance. Emerging techniques such as pCLE and OCT enable real-time, *in vivo*, endohistologic assessment, but additional study is needed to standardize interpretation, improve inter-rater reliability, and validate performance. The challenges in diagnosis often result in multimodal testing that marginally enhances diagnosis but substantially increases cost. While application of new and innovative technologies is of interest to endoscopists, their use must be tempered by the realization of only marginal improvements in diagnostic sensitivity and frequent decrement in specificity, their potential for adverse events, associated cost, and often limited availability to a small number of diagnostic centers. In addition, more research is needed to determine how to best guide important clinical decisions using these and other established and emerging modalities.

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Achieving competence in colonoscopy: Milestones and the need for a new endoscopic curriculum in gastroenterology training

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Abstract

Colonoscopy is considered to be the most effective tool for reducing colorectal cancer (CRC) morbidity and mortality. As a result, certifying trainee competence in the performance of colonoscopy is critical to maximizing CRC screening and prevention efforts. Guidelines on training and accreditation around the world have been revised to emphasize the attainment of milestones in the technical and cognitive skills necessary to perform the procedure. To meet this challenge, new evaluation systems have been developed to measure trainee competence through all aspects of colonoscopy training. These changes stem from increased recognition that procedural numbers alone do not necessarily guarantee trainees' proficiency in the performance of colonoscopy. Variability in endoscopic practice and in CRC screening outcomes also point to deficiencies in the current approach towards colonoscopy instruction. However, technological innovations hold great promise in training endoscopists to perform high quality colonoscopy. Furthermore, potential advances in the use of feedback as a training tool provide new avenues for research. This review summarizes the latest evidence on the effort to define, evaluate and promote the achievement of competence in colonoscopy among trainees.

Key words: Competence; Colonoscopy; Colorectal cancer; Core curriculum; Cecal intubation

Core tip: The certification of competence among trainees in the performance of colonoscopy is currently evolving. Recent efforts are shifting the paradigm towards formal evaluation systems that emphasize core skills. Similar innovations in technology and teaching methods provide the push to re-define the future curriculum for colonoscopy training.

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INTRODUCTION

The process of determining if medical trainees possess the requisite knowledge and skill to practice the healing arts has played a central role in the evolution of medicine. In the time of the ancient Greeks and Romans, competence was based upon the judgment of the elder physician under whom the trainee served as an apprentice[1]. In 1260, the Mongol Emperor Kublai Khan established the first system of certification based upon the completion of formal written examinations[1]. With the founding of the Royal College of Physicians in London in 1518, a further shift towards formal medical licensure took place with the advent of both written tests and objective assessments of procedural skills[1].

In gastrointestinal endoscopy, the task of certifying competence among trainees is also evolving from an apprenticeship model towards a more objective process based upon the achievement of milestones. With nearly 14.2 million procedures performed in the United States alone[2], colonoscopy represents the most common endoscopic procedure performed by gastroenterologists, surgeons and family practitioners. However, recent studies suggest that the detection of adenomatous polyps and the development of missed interval colorectal cancers (CRCs) may be closely related to the proficiency of the endoscopist[3-5]. Consequently, the process by which trainees are trained and certified to be competent in the performance of colonoscopy has become a high priority.

To approach this vital issue, there are several salient questions to be asked: (1) What is competence; (2) Why does competence matter; (3) How do we determine trainee competence; (4) Do trainees currently attain competence; and (5) How do we help trainees to attain competence.

WHAT IS COMPETENCE?

Competence is defined by the American Society for Gastrointestinal Endoscopy (ASGE) as the "Minimal level of skills, knowledge and/or expertise derived through training and experience that is necessary to safely and proficiently perform a task or procedure"[6]. Competence is determined to be contingent upon: (1) Technical skills to safely perform the procedure; and (2) Cognitive skills to take information gained from a procedure and to place it in the appropriate clinical context[6]. These cognitive and technical skills are further broken down into basic and intermediate competencies (Table 1)[7].

Given that the end-goal of colonoscopy is to reduce CRC-related mortality, competence among trainees can also be defined based upon their ability to surpass quality thresholds. The ASGE defines these benchmarks as: (1) adenoma detection rate (ADR) of $\geqslant$ 30% in male and $\geqslant$ 20% in female patients undergoing average-risk CRC screening; (2) A successful cecal intubation of $\geqslant$ 90% in all colonoscopies and $\geqslant$ 95% for screening colonoscopy; (3) the successful removal of polyps < 2 cm in size; and (4) A colonoscopy withdrawal time of > 6 min[8]. In the United Kingdom, the Joint Advisory Group (JAG) on gastrointestinal (GI) endoscopy requires: (1) Cecal intubation rate of > 90%; (2) > 90% of rate of completing procedures without assistance; (3) Attendance at a basic skills colonoscopy course; and (4) Procedure total of $\geqslant$ 200[9].

WHY DOES COMPETENCE MATTER?

While the answer to this question may seem largely self-evident, the process of certification is salient to many potential interests regarding colonoscopy. First and foremost, endoscopist competence has been shown to have a significant impact on the effectiveness of colonoscopy in detecting and preventing CRC. Baxter *et al*[4] recently questioned the long-standing assumption that colonoscopy decreases CRC-related morbidity and mortality when they demonstrated that the procedure was not protective for right-sided CRC (OR = 0.99, 95%CI: 0.86-1.14). To potentially explain this observation, Singh *et al*[10] in a large population based study in Manitoba, Canada found that colonoscopy with polypectomy, cecal intubation failure and procedures performed by family practitioners were associated with the development of interval CRC within 3 years of an index colonoscopy. This raises the prospect that low levels of competence in polypectomy, cecal intubation and endoscopic training limit the effectiveness of colonoscopy. Furthermore, Kaminski *et al*[11] found that endoscopists with a mean ADR of < 11% had a cumulative hazard rate for the development of interval CRC of 10.94 (95%CI: 1.37-87.01) when compared with physicians who had an ADR of > 20%. A similar study by Corley *et al*[12], found that physicians who increased their ADR from the lowest quintile to the highest quintile prevented 1 interval CRC over the course of 10 years. Furthermore, they found that every 1.0% increase in ADR predicted a 3.0% decrease in the risk of interval cancer (HR = 0.97; 95%CI: 0.96-0.98)[12]. Given that ADR is one of the primary benchmarks for both competence and quality in colonoscopy, it is clear that the process of determining endoscopist proficiency plays a pivotal role in the effort to improve CRC prevention.

Finally, the issue of establishing competence among trainees is important because of recent studies that demonstrate that physician behavior is difficult to alter once an endoscopist is no longer a trainee. Sawhney *et al*[13] found that an institutional mandate to achieve a minimum withdrawal time (time spent from cecal intubation to removal of the colonoscope from the anus) among 42 attending endoscopists failed to produce any significant change in polyp detection rate (PDR). Lin *et al*[14] performed a similar study where they provided periodic feedback of patient satisfaction scores, average withdrawal time, and PDR every 3-6 mo to 10 attending gastroenterologists who were at least 8 years removed from training. One year after the implementation of this feedback mechanism, there was no significant increase

Table 1 American Society for Gastrointestinal Endoscopy Core Curriculum list of core motor and cognitive skills required to be competent in colonoscopy[7]

Motor	Cognitive
Correctly holding the colonoscope	Anatomy
Use of the colonoscopy controls	Patient selection
Colonoscope insertion	Preparation
Colonoscope advancement	Colonoscope selection
Tip control	Informed consent
Torque	Sedation management
Lumen identification	Assessment of indication and risks
Withdrawal/mucosal inspection	Pathology identification
Loop reduction	Therapeutic device settings
Angulated turns	Integration of findings into management plans
Terminal ileum intubation	Report generation and communication
Biopsy	Complication management
Snare polypectomy	Quality improvement
	Professionalism

in either PDR (33.1% *vs* 38.1%, P = 0.04) or ADR (19.6% *vs* 22.7%, P = 0.17)[14]. These observations highlight the potential value of establishing good practices early on in the career of an endoscopist.

HOW DO WE DETERMINE TRAINEE COMPETENCE?

Traditionally, credentialing guidelines have focused primarily on the number of colonoscopies performed to determine procedural competence. In a small study of 7 trainees (4 GI fellows, and 3 surgical residents), Freeman *et al*[15] defined competence based upon independent cecal intubation. They found that trainees were able to intubate the cecum without assistance only 80% of the time after the first 50 procedures and consequently concluded that > 100 cases were likely required to achieve a 90% success rate. Using a cecal intubation time of < 15 min, a cecal intubation rate > 90%, and a 6-point technical skill score as a measure of competence, Chak *et al*[16] found that trainees did not achieve an attending-level of proficiency in colonoscopy even after 120 procedures were performed. These observations form the basis for the Accreditation Council for Graduate Medical Education (ACGME) and ASGE recommendation that a trainee perform a minimum of 140 cases before competency can be assessed in colonoscopy[6,17]. The European Board of Gastroenterology, the Canadian Association of Gastroenterology and the Conjoint Committee for the Recognition of Training in Gastrointestinal Endoscopy in Australia however use the 100 case threshold[18-20]. In the United Kingdom, JAG guidelines recommend a higher threshold (200 independently completed colonoscopies)[9].

Recently, several studies have highlighted the fact that these numbers represent a minimal threshold for competence and that procedural numbers by themselves do not guarantee trainee proficiency. In a large study involving 15 tertiary care centers in South Korea, Lee *et al*[21] found that trainees were able to independently intubate the cecum > 90% of the time, and attain a cecal intubation time of < 20 min only after > 150 procedures were performed. Spier *et al*[22] defined competence as the point at which trainees were able to perform all aspects of colonoscopy (cecal intubation, polypectomy, hemostasis) without the aid of an attending > 90% of the time. Using this definition, the investigators found that all of the 11 GI fellows studied attained these objectives by 500 cases but none attained that goal by the 140 case threshold set by the ASGE/ACGME guidelines[22]. And in a multicenter study[23] of 7 first-year GI fellows at two separate training programs, our own group sought to determine the threshold number of cases at which trainees were able to achieve: (1) Independent cecal intubation rate of $\geqslant$ 90%; (2) Independent ADR of $\geqslant$ 25%; (3) Mean withdrawal time $\geqslant$ 6 min; and (4) Ability to successfully remove polyps without the aid of the attending $\geqslant$ 95% of the time. This study was unique in that nurses were asked to judge whether each of the skills (adenoma detection and removal, cecal intubation) were performed by the fellow without significant assistance by the attending. Consequently, trainees were given credit for adenoma detection only if the adenoma was determined to be independently detected and removed by the trainee in the opinion of the endoscopy nurse. Using these criteria, we found that trainees achieved all of the quality benchmarks only when 201-250 procedures were performed[23].

Recognizing the inherent shortcomings in assigning competence solely based upon procedural numbers, recent efforts have focused on developing evaluation systems that assess both the technical and cognitive skills necessary to perform colonoscopy. In the United Kingdom, the JAG group has developed the Direct Observation of Procedural Skills (DOPS) evaluation for colonoscopy as part of a national system of accreditation for GI trainees[24]. Using a 4 point scoring system ranging from 1-Accepted standards not yet met; frequent errors uncorrected to 4-highly skilled performance, assessors are tasked with grading trainees on both diagnostic and therapeutic skills in colonoscopy. In a study of 111 attending endoscopists, Barton *et al*[24] demonstrated that DOPS had good relative reliability (G = 0.81) and a good correlation with a questionnaire that assessed candidates' knowledge. While the value of DOPS as a method for determining trainee competence is yet to be validated, current JAG guidelines require a total of 10 DOPS evaluations with > 90% of them having no score less than 3 for any given skill. A similar scoring system known as the Direct Observation of Polypectomy Skills (DOPyS) has also been developed by JAG to determine competence in polyp removal using the same four point rating scale with scores of 1-2 considered as failing grades[25]. In a study by Gupta *et al*[25], DOPyS was found to have discriminatory value in differentiating experienced endoscopists with > 1000 procedures from GI trainees who had limited experience in therapeutic

colonoscopy. The added advantage of the DOPyS rating system is that it has been validated to be applied towards video-recordings of procedures.

In the United States, Sedlack[26] have made significant strides in the development of a comprehensive evaluation system for determining trainee competence with the advent of the mayo colonoscopy skills assessment tool (MCSAT). Using a rating system of 1 (Novice) to 4 (Superior), the MCSAT evaluates trainees during live cases[26]. Trainees are assessed in terms of cognitive skills such as knowledge of indication for procedure, use of initial sedation, landmark localization, and pathology identification. They are also are evaluated on procedural abilities such as safe endoscope advancement techniques, loop reduction, mucosal visualization during withdrawal, and polypectomy. In a large study of 41 GI fellows who were evaluated during 4103 procedures, the investigators determined that a mean score of $\geqslant$ 3.5 in all MCSAT parameters along with a cecal intubation rate of 85% and a mean cecal intubation time of less than 16 min best distinguished experienced endoscopists from trainees who had not yet met minimal competence thresholds[27]. Furthermore, they found that GI fellows did not reach these goals until 275 procedures were performed[27]. Because of this work, the most recent ASGE Core Curriculum has endorsed using the MCSAT as a tool for competency assessment throughout colonoscopy training[7].

DO TRAINEES CURRENTLY ATTAIN COMPETENCE?

While there are no formal studies outlining the characteristics of colonoscopy training among Gastroenterology, Surgery and Family Practice programs, it is highly probable that a large degree of variability exists in the educational approaches taken towards teaching trainees how to perform the procedure. Teaching strategies likely vary with the "See one, do one, teach one" approach on one end of the educational spectrum and more didactic and hands-on instruction by an experienced endoscopist on the other. This heterogeneity in training is highlighted by studies that compare GI trainees and surgical residents in achieving benchmarks in quality colonoscopy. In a study of 7 GI fellows and 6 surgical residents, Leyden *et al*[28] found that surgical trainees had lower cecal intubation rates (84% *vs* 93%, $P < 0.0001$), polyp detection rates (14% *vs* 21%, $P < 0.0001$) and ADR (9% *vs* 14%, $P = 0.0065$). A similar study by Spier *et al*[29] found that surgical residents only had a cecal intubation rate of 47% after a mean of 80 procedures were performed.

Even among trainees in recognized GI fellowship programs, recent studies point to potential deficiencies in the approach towards teaching colonoscopy. In an innovative tandem colonoscopy among procedures performed by GI fellows, Munroe *et al*[30] found an overall adenoma miss rate of 27%. Furthermore, the investigators found that there was a 2.2 fold decrease in the risk of missing an adenoma with each 10 fold increase in trainee experience[30]. Thus, to attain a less than 25% adenoma miss rate, a trainee would have to perform 450 procedures, a number that many GI fellows and certainly most surgical and family practice trainees may never reach in the course of training. One potential explanation for this finding is a failure to fully incorporate quality guidelines into the educational curriculum on the part of many training programs[30]. In an online survey on quality guidelines for colonoscopy, GI fellows received a mean score of 55% correct, with only 42% identifying the correct cecal intubation rate goal and 44% indicating the correct ADR benchmark[31].

Finally, feedback from GI trainees themselves highlight the need for improvements in colonoscopy instruction. In a survey of 169 GI trainees in the United Kingdom, Wells *et al*[32] found that only 36% felt that they were "fully" trained in colonoscopy. Furthermore, the respondents estimated than an attending was in the room to provide supervision in only 30% of colonoscopies that were performed[32]. Trainees also cited important aspects of effective teaching which included: (1) Close interaction with a supervisor who has good teaching skills; (2) Systematic approach towards endoscopic techniques; (3) Excellent supervision and discussion-based training; (4) Attendance of a course on quality colonoscopy; and (5) Smaller procedure schedules to allow for training time[32]. These comments point to the need for reforming our current approach toward teaching colonoscopy.

HOW DO WE HELP TRAINEES ATTAIN COMPETENCE?

Advances in both technology and teaching methods clearly point the way towards a new curriculum that is based upon establishing competence in colonoscopy. From a technological standpoint, innovations in simulation present new avenues for trainees to develop and hone cognitive and technical skills away from the time pressures and risks of performing procedures on live patients. Current simulators consist of a mannequin and a modified colonoscope with pressure sensors which mimic the resistance felt with scope advancement and loop formation. Trainers are able to assign specific modules to trainees on the simulators ranging from basic lessons meant to establish hand-eye coordination skills to more realistic scenarios in which full cases are performed on simulated patients.

Several randomized controlled trials have demonstrated a potential benefit to the use of simulation during the early phase of colonoscopy training. Cohen *et al*[33] compared simulation (Simbionix GI Mentor, Simbionix Corporation, Cleveland, Ohio) *vs* non-simulation trained GI fellows in terms of competence measures on colonoscopies performed on live patients. In particular they looked at subjective (rating scale of 1-5 on the part of the trainer) and objective measures such as successful cecal intubation and the ability to correctly identify

Table 2 Median performance scores (25%-75% interquartile range) on live-patient procedures among fellows trained on colonoscopy simulator *vs* trainees with bedside training alone[34]

Fellow performance parameters	Simulator fellow (n = 462)	Traditional teaching (n = 423)	P value
Time to reach maximum insertion (min)	20.0 (14.0-25.0)	20.0 (15.0-29.8)	0.170
Median depth of unassisted insertion (1 = rectum, 6 = terminal ileum)	5.0 (4.0-6.0)	5.0 (4.0-5.0)	0.002
% of colonoscopies completed independently	64.1% (59.7-68.5)	56.3% (51.6-61.0)	0.018
Identifies landmarks (1 = strongly disagree, 7 = strongly agree)	7.0 (6.0-7.0)	6.0 (6.0-7.0)	0.003
Inserts in a safe manner (1 = strongly disagree, 7 = strongly agree)	7.0 (6.0-7.0)	7.0 (6.0-7.0)	0.020
Adequately visualizes mucosa during withdrawal	7.0 (6.0-7.0)	6.0 (6.0-7.0)	0.009
Responds appropriately to patient discomfort	7.0 (6.0-7.0)	6.0 (6.0-7.0)	0.255
Patient-reported discomfort	1.0 (1.0-4.0)	1.0 (1.0-4.0)	0.090

cecal landmarks[33]. During the first 80 live cases, the simulator-trained group had higher objective and subjective levels of competence[33]. However after 120 cases, the advantage found with simulation was no longer present and both groups still required a total of 160 live cases to attain 90% competence[33]. In a similar study by Sedlack *et al*[34], GI fellows who received training using the AccuTouch Colonoscopy Simulator (Immersion Medical, Gaithersburg, MD) scored better on all performance measures (Table 2) except for cecal intubation time when compared with trainees who received just bedside instruction on live patients. However, the differences between the two groups also dissipated once greater than 30 procedures were performed[34]. The positive impact of simulation during the early phases of colonoscopy instruction is well summarized in a meta-analysis by Walsh *et al*[35] who found that there was a significant benefit when simulator-based training was compared to no-training at the beginning of fellowship. In contrast, the advantage of simulator-based training was less pronounced when it was pitted against usual training on live patients[35].

Along with simulation, recent advances in technologies designed to be used during live-cases also hold promise in helping trainees to achieve competency in colonoscopy. During training, the formation and reduction of loops that occur with scope advancement represent one of the most important skills that a trainee must acquire in order to safely perform colonoscopy. To assist in this task, magnetic endoscope imaging (MEI) has been developed to provide trainees with a real-time view of scope positioning. With the ScopeGuide (Olympus Corporation, Tokyo, Japan) MEI system, coils embedded within the colonoscope generate an electromagnetic field which is detected by an external receiver dish producing a 3-dimensional image of the location of the colonoscope[36]. In a randomized controlled trial comparing MEI assisted *vs* standard colonoscopy Shah *et al*[37] found that trainees who performed with MEI had a shorter duration of loop formation (median 3 min *vs* 5.4 min, P = 0.0049) and a fewer number of loop straightening attempts (5 *vs* 12, P = 0.0002). In a similar study of trainees who had experience of fewer than 200 procedures, Holme *et al*[36] observed a higher rate of cecal intubation (77.8% *vs* 56%, P = 0.022) and a lower percentage of cases which required attending assistance (18.5% *vs* 40%, P = 0.018) in the MEI group. Thus, MEI may provide a useful role in colonoscopy training if it aids trainees in acquiring the feedback response for recognizing loop formation.

Water immersion colonoscopy also represents another more readily available modality which may assist trainees in their development of procedural competence. In the early stages of training, novices often have difficulty in discerning the direction of the lumen and as a result this leads to prolonged cecal intubation time, the excessive insufflation of air into the colon, looping of the colonoscope and patient discomfort. Addressing these issues, the water immersion technique refined by Leung *et al*[38] involves filling the colonic lumen with room temperature or warm water using a pump connected to the colonoscope. The air pump is turned off during the intubation phase and 30-60 cc of water is instead used to open the collapsed lumen[38]. In a randomized controlled trial by Leung *et al*[39], trainees who used water immersion had shorter cecal intubation times (13 min *vs* 20.5 min, P = 0.0001), lower mean doses of midazolam (mean dose 2.41 mg *vs* 2.9 mg, P = 0.001) and Fentanyl (mean dose 37.9 mcg *vs* 71.7 mcg, P = 0.002) than those who utilized standard air insufflation. More importantly, a recent meta-analysis found that water immersion resulted in higher ADR (RR = 1.16, 95%CI: 1.04-1.30, P = 0.007) and would lead to an additional 68000 colonoscopies in the United States where an adenoma is detected[40].

Along with water immersion, hood-assisted colonoscopy may also aid trainees in determining the direction of the lumen with scope insertion. Because novice endoscopists often have poor control of scope movement and directionality, a significant amount of time is spent with a "redded-out" image because the scope tip is stuck against the colonic wall[41]. This leads to prolonged scope insertion time and excessive air insufflation. A transparent hood that is attached to the instrument tip may help with this problem by maintaining a proper distance between the colonoscope camera and the colonic mucosa. Furthermore, the hood may assist in mucosal inspection and polyp detection upon withdrawal since it helps with depressing and exposing colonic folds. In a randomized trial of hood colonoscopy *vs* standard colonoscopy among Italian trainees, the hood group was found to have a shorter cecal intubation time (4.4 ± 1.8

vs 7.3 ± 3.5, $P < 0.01$), and a higher rate of detecting polyps 5 mm-1 cm in size (72% *vs* 44%, $P = 0.01$)[41]. A similar randomized controlled trial in Japan, found that trainees had a higher cecal intubation rate (60.7% *vs* 37.4%, $P = 0.003$) among female patients and a 17% reduction in cecal intubation time when hood-assisted colonoscopy was used[42]. Consequently, hood-assisted colonoscopy and water immersion both hold promise as future techniques in colonoscopy training if they assist trainees in the sustained acquisition of skills in luminal orientation, safe scope advancement and polyp detection.

While technology may prove to be important in shaping the future of colonoscopy instruction, the role of feedback will remain the central foundation of the colonoscopy core curriculum. The ASGE Training Committee guidelines recommend that: "Regardless of the method ultimately used, it is recommended that some form of continuous assessment be performed and the results used ideally in a formative manner- to give feedback to trainees in areas where further work may be needed-and a summative assessment of skills that can be used for competency assessment"[7].

Despite this directive, the utility of assessment and feedback as teaching tools in colonoscopy remains poorly understood. Koch *et al*[43] developed a self-assessment form (Rotterdam Assessment Form) which asked trainees to rate their own performance after completion of individual procedures. The form consisted of objective data including successful cecal intubation, cecal intubation time, and the amount of time spent without attending assistance along with a subjective rating of various colonoscopy skills using a visual analogue scale and an action plan for improvement[43]. After the implementation of this self-evaluation system, the cecal intubation rate improved from 65% after the first 20 procedures to 85% at 200 procedures ($P < 0.001$)[43]. Cecal intubation time also improved from 13 min, 10 s at 20 procedures to 8 min 30 s after completion of 200 colonoscopies[43]. However, even with these results, it remains largely unclear if the self-evaluation system resulted in an actual improvement on the normal rate of skills acquisition or improvements in polyp detection that one would see in the regular course of training.

While the clinical evidence for using feedback as a training tool in colonoscopy remains limited, this area provides fertile ground for future research endeavors. In a study by Rex *et al*[44] the act of video-recording individual colonoscopies resulted in a 49% improvement in mucosal inspection time and a 31% improvement in withdrawal technique among experienced endoscopists. Relying upon the concept of the Hawthorne effect whereby subjects improve or modify their behavior in response to the fact that they are being studied[45], it is certainly possible that video-recordings can be used to improve technical and cognitive performance among trainees. Furthermore, the addition of the MCSAT to the colonoscopy core curriculum also affords the opportunity to use continuous feedback of competency scores and comparisons with the group average to assist novices in identifying areas that require improvement. Finally, the current JAG certification process also requires trainees to provide a formal assessment of the trainers' performance during individual procedures. Similar "train the trainer" measures that seek to improve the quality of colonoscopy instruction are vitally important from both research and educational standpoints.

CONCLUSION

While the process of certifying competence has clearly evolved away from the apprenticeship model of medical training, the future shape of colonoscopy instruction remains to be determined. With the increasing emphasis on quality benchmarks and recent data questioning the pre-eminent role of colonoscopy in CRC screening due to variability in endoscopic practice, the task of evaluating and teaching competence remains as important as ever. The movement away from concentrating on procedural numbers and towards the attainment of milestones in the development of cognitive and technical skills represents a significant shift in determining competence in colonoscopy. As first steps in this evolution, the MCSAT and the DOPS evaluation systems standout as significant contributions to the process of re-defining the core curriculum. Whether the solution lies in better technology or a feedback-based system of procedural instruction, the approach towards educating trainees will need to adapt to a curriculum that rightfully emphasizes the importance of quality colonoscopy.

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Role of virtual reality simulation in endoscopy training

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Abstract

Recent advancements in virtual reality graphics and models have allowed virtual reality simulators to be incorporated into a variety of endoscopic training programmes. Use of virtual reality simulators in training programmes is thought to improve skill acquisition amongst trainees which is reflected in improved patient comfort and safety. Several studies have already been carried out to ascertain the impact that usage of virtual reality simulators may have upon trainee learning curves and how this may translate to patient comfort. This article reviews the available literature in this area of medical education which is particularly relevant to all parties involved in endoscopy training and curriculum development. Assessment of the available evidence for an optimal exposure time with virtual reality simulators and the long-term benefits of their use are also discussed.

Key words: Virtual reality; Colonoscopy; Sigmoidoscopy; Endoscopy; Endoscopic ultrasound; Medical education; Endoscopic retrograde cholangio-pancreatography; Gastroscopy; Simulation

Core tip: There is good evidence for the use of virtual reality simulation in endoscopy training programmes, with most benefit seen amongst novice trainees. More research is needed concerning the best integration of simulators within a training programme and the optimal exposure needed. Findings are limited by the variety of simulators used and limited power of the studies. More evidence is also needed to support the benefits virtual reality simulators may have within endoscopic ultrasound and endoscopic retrograde cholangio-pancreatography training programmes.

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INTRODUCTION

Endoscopy training and skill acquisition conventionally involves observation and feedback on a trainee's performance under the supervision of an experienced endoscopist. This applies to traditional training in a variety of procedures, including oesophagogastroduodenoscopy (OGD), endoscopic retrograde cholangiopancreatography (ERCP), endoscopic ultrasound (EUS) and colonoscopy. More recently, a variety of alternative educational tools have become available that aim to improve trainees' endoscopy skills.

Virtual reality (VR) simulators are an educational modality that has been purposely developed to facilitate endoscopy training in a controlled environment. With improving graphics and technology, medical simulation has advanced from basic mechanical models or animal models to screen-based simulators. Their use and incorporation into endoscopy training curricula has been thought to enhance the speed of trainee skill acquisition, thus improving patients' comfort and safety during candidates' initial phase of learning[1].

This review article aims to evaluate existing evidence on the role of VR simulation in endoscopy training, identify if there is an evidence-based educationally optimal method of incorporating such simulators within endoscopy training programmes and to review the impact that VR simulator training may have upon patient comfort. This article will focus on the impact of virtual reality simulator training for the most common endoscopy modalities, namely OGD, ERCP, EUS and colonoscopy.

LITERATURE STUDY

An extensive bibliographical search was performed *via* the online databases MEDLINE and EMBASE using the following keywords: Simulation, simulator, virtual reality, endoscopy, gastroscopy, OGD, colonoscopy, sigmoidoscopy, endoscopic retrograde cholangio-pancreatography, ERCP, endoscopic ultrasound, EUS. Some of these terms (simulation, simulator, virtual reality), which were relating to simulation, were searched in combination with the remaining keywords, which were relating to endoscopy (*e.g.,* "simulation and endoscopy", "simulation and colonoscopy", "virtual reality and gastroscopy", *etc.*), in order to identify all relevant papers investigating the role of virtual reality simulation in endoscopy training. The results were combined before duplicates were removed and the reference lists from the selected studies were manually examined to identify further relevant reports.

All primary research papers published in full from any year of publication were considered for inclusion in this review, regardless of their design. These papers included internationally conducted studies, but only those written or translated into English were included in the full text assessment. The participants of studies considered in this review ranged from physicians, nurses and medical students and the individuals' endoscopy experience was not taken into account in screening for studies. The intervention sought was that of VR endoscopy against traditional patient-based training methods or where there was no comparison at all.

Screening of these results removed papers which did not have an educational impact focus, as well as discussion papers, in which the title and abstract aimed to legitimise VR simulators (in comparison to traditional training) solely by expert opinion. Papers that included non-VR educational simulators which involved *ex-vivo* parts or mechanical models were also excluded. This demonstrated that a subset of 24 articles were relevant for this review (Figure 1).

RESULTS

Role of VR simulation in OGD training

Table 1 shows the methodology of the eight studies that were included.

Regarding the role of VR simulators in OGD training the available evidence demonstrates that screen-based simulators have a useful role in facilitating training of novice candidates in OGD[2-7], and potentially a place in the continued professional development of more experienced trainees[2,6,8].

Multiple studies have shown that novice trainees who underwent training that included a VR simulator had significantly better performance outcomes than candidates who were traditionally trained in OGD[3-5,7] and Table 2 summarises the various outcomes of studies investigating the role of VR simulation in OGD training. Ferlitsch *et al*[7] furthered support for early use of the VR simulators by showing that there was a continued significant difference in VR simulator-trained candidates' timing, diagnostic and technical accuracy at 60 d. The only study to report a negative outcome comparing simulator training against traditional training stated that the incidence of pain was reported as higher amongst those who used the simulator[9].

Another study showed that a significant proportion of trainees who utilised VR simulators felt that simulator practice would be most useful in early training, with those who were more advanced reporting that some of the modules were not very realistic for their stage of training[6].

Role of VR simulation in ERCP training

Although there have been several studies looking into the role of simulation in ERCP training, the majority of these have used mechanical models and only one has focused on the role of VR simulation. This study enrolled novice and expert endoscopists and aimed to determine the construct and face validity of the simulator. It concluded that the GI Mentor Ⅱ simulator was both realistic and able to differentiate novices and experts based on their performance. In addition, most participants considered it a helpful training tool[10]. Table 3 provides a summary of the design and outcomes of

Table 1 Summary of analysed oesophagogastroduodenoscopy studies and their design

Ref.	No. of participants	Participants' level of training	Design	Task	Model	Primary outcome	Secondary outcomes
Bloom *et al*[6]	35	Novice and advanced	NRSIS	Visualisation Questionnaire	5 DT gastroscope training simulator	Time to complete procedure[1]	Wall visualisation[1] Questionnaire responses
Clark *et al*[2]	13	Novice and advanced	NRSIS	Completion of monthly assignments over two years on simulator	GI Mentor Ⅰ	Objective criteria measured by simulator[1]	
Di Giulio *et al*[4]	22	Novice	MC RCT	Complete simulator or control training programme	GI Mentor Ⅰ	Competency scores[2]	Instructor assessed[2]
Ferlitsch *et al*[7]	13	Mixed novice and advanced	RCT	Comparison of novice and expert performance in simulated endoscopy. Comparison of performance of simulation-trained and control group of novices	GI Mentor Ⅰ	Competency scores from simulator[1]	
Ferlitsch *et al*[3]	28	Novice	RCT	Training on simulator against traditional training	GI Mentor Ⅰ	Competency scores from expert after 10 and 60 endoscopic examinations[2]	Pain experienced by patient
Sedlack[9]	8	Novice	RCT	6 h simulation training before 1 mo of traditional training	GI Mentor Ⅱ	Mixed competency scores from expert[2]	
Shirai *et al*[5]	20	Novice	RCT	5 h simulation training before 2 assessed endoscopies	GI Mentor Ⅱ	Mixed competency scores from expert[2]	
Van Sickle *et al*[8]	41	Mixed novice and advanced	MC NRSIS	Baseline assessment on simulator and after 8 wk of training	GI Mentor Ⅱ	Competency scores from expert[1]	

[1]Simulator-related outcome; [2]Patient-related outcome. MC: Multicentre; RCT: Randomised control trail; NRSIS: Non-randomised single-intervention study; GI: Gastro-intestinal; DT: Dimension technologies.

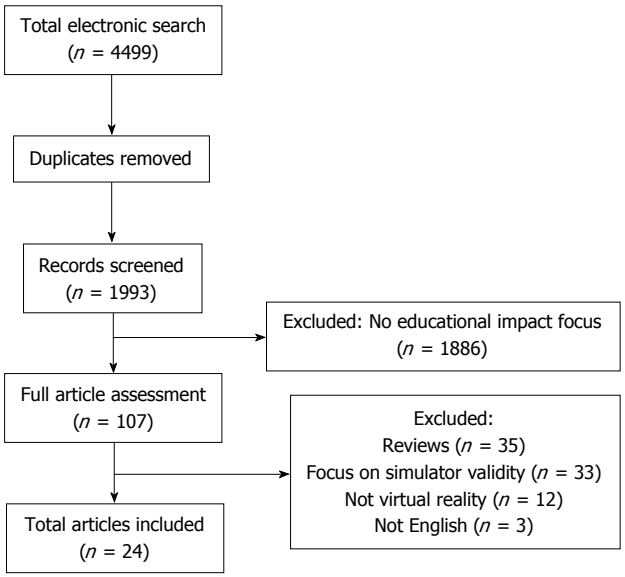

Figure 1 Article screening and selection process.

this study.

Role of VR simulation in EUS training

Only one study could be found that discusses the role of VR simulation in EUS training[11]. Eight experts compared an EUS VR simulator (EUS Mentor) to an animal model, a phantom (EUS FNA box) and a combination model and ranked them by realism, utility as an educational modality, ease of use and ease of incorporation into a training programme. They determined the phantom model to be easiest to use and incorporate into training, whereas animal models were marked as best for realism and utility as an educational tool[11].

Role of VR simulation in colonoscopy training

Table 4 shows the methodology of the thirteen studies that were included.

In assessing the role of VR simulators in colonoscopy training there is more evidence to support its use in training programmes[12-21]. In one survey, 91% of all participating candidates agreed that VR simulators would be useful in their training[12]. Several studies demonstrated that when VR simulator training was compared to traditional colonoscopy training alone, competency parameters were significantly greater amongst simulator trained candidates[13,15-18,20]. The majority of these studies adopted the same methodology, utilising the VR simulator model before candidates started traditional training, which supports the use of VR simulators in this way.

Some studies attempted to determine the amount of exposure with the simulator which is necessary to acquire an "expert" skill base - determined when learning curves plateaued on the simulator modules. While one study reported that the learning curve of novice candidates plateaued on the seventh consecutive attempt[22], another stated that learning curves consistently plateaued at or after the ninth attempt amongst novice candidates[23]. In a separate study which compared learning curves between novice residents and nurses with varying experience in endoscopy the learning curve

Table 2 Results of studies evaluating the role of simulation in oesophagogastroduodenoscopy training

Ref.	Primary outcome	Secondary outcome
Bloom *et al*[6]	Mean time to complete procedure was 224 ± 27.65 s for novice, 171.22 ± 25.43 s for intermediate and 106.40 ± 13.08 s for experienced candidates (P = 0.008) The study demonstrated the construct validity of the simulator	Mean percentage of total surface visualised was 60.56 ± 2.56 for novice, 66.56 ± 2.80 for intermediate and 72.10 ± 0.23 for experienced candidates (P = 0.005) Questionnaire responses suggested that novice and intermediate candidates considered VR simulation an important training tool
Clark *et al*[2]	Efficiency scores (total time to complete procedure divided by percentage of mucosal surface examined) of senior residents were higher than those of junior residents (85% *vs* 59%) demonstrating improved efficiency with continued use of simulator	
Di Giulio *et al*[4]	The simulator-trained group performed a higher number of complete procedures (87.8% *vs* 70%, P < 0.0001) and needed less assistance (41.3% *vs* 97.9%, P < 0.0001) compared to control group. Length of procedure was similar in the two groups	Instructor marked performance as positive more frequently in the simulator-trained group compared to the controls (86.8% *vs* 56.7%, P < 0.0001)
Ferlitsch *et al*[7]	Performance of expert candidates (compared to novices) was better in performance of J-manoeuvre during oesophagogastroduodenoscopy (P < 0.005), complications at colonoscopy (P < 0.02), insertion time (P < 0.001), identification of abnormal findings in gastroscopy and colonoscopy (P < 0.02) and skill performance (P < 0.01). Amongst novices, the simulation-trained group had a better performance compared to the controls in relation to complication rates at virtual endoscopy (P < 0.04), the insertion time during colonoscopy (P < 0.03) and skill performance (P < 0.01)	
Ferlitsch *et al*[3]	The simulation-trained group performed better than the control group in terms of time needed to reach the duodenum [239 s (range 50-620) *vs* 310 s (110-720), P < 0.0001] and technical ability (P < 0.02) in the first ten endoscopic examinations on patients. Diagnostic ability was similar in the two groups After 60 endoscopic examinations, investigation time was still less in the simulation-trained group. Technical and diagnostic ability improved during on-patient training in both groups and differences between groups were no longer seen at that stage	There were no significant differences in pain scores between the groups after 10 and after 60 endoscopies
Sedlack[9]	The control group performed better than the simulation-trained group in terms of patient discomfort (5; IQR, 4-6 *vs* 6; IQR, 5-6; P = 0.015), sedation, independence and competence scores	
Shirai *et al*[5]	The simulator-trained group achieved significantly higher scores than the control group in the following skills: oesophageal intubation, passing from the EGJ to the antrum, pyloric intubation, and examination of the duodenum and the fundus	
Van Sickle *et al*[8]	The study group showed an improvement in endoscopic skills (*e.g.*, Global Assessment of Gastrointestinal Endoscopic Skills scores) after 8 wk of VR simulation training	

IQR: Interquartile range; EGJ: Esophagogastric junction; VR: Virtual reality.

Table 3 Summary of analysed endoscopic retrograde cholangio-pancreatography study and its design

Ref.	No. of participants	Participants' level of training	Design	Task	Model	Primary outcome	Secondary outcomes
Bittner *et al*[10]	12	Mixed	NRSIS	2 simulator ERCP cases	GI Mentor Ⅱ	Time to complete procedure[1]	Time to papilla[1] Questionnaire on views

[1]Simulator-related outcome. NRSIS: Non-randomised single-intervention study; ERCP: Endoscopic retrograde cholangio-pancreatography; GI: Gastro-intestinal.

did not plateau in any group by the tenth attempt[21].

In addition, several studies evaluated the effect of VR simulation training on patient discomfort. Most studies found that this was less during the procedure in simulator trained candidates[13,14,18], but few concluded that there was no significant difference between the two groups[15,24].

Better evidence that simulator training has effective translational skills can be identified by the long-term impact that simulator training has on a candidate's skill base. It has been shown that a simulator trained candidate retains a significant advantage in competence during their first 100 colonoscopies[15] and that these skills are maintained 9 mo after the simulator intervention[19].

Such concordance advocates strong support for the use of simulators in endoscopy training. However, it is important to note the findings in Gerson *et al*[24] which

Table 4 Summary of analysed colonoscopy studies and their design

Ref.	No. of participants	Participants' level of training	Design	Task	Model	Primary outcome	Secondary outcomes
Aabakken *et al*[12]	33	Mixed	NRSIS	1 simulated colonoscopy and questionnaire	GI Mentor	User satisfaction[1]	
Ahlberg *et al*[13]	12	Novice[3]	RCT	Completion of simulator or control training programme followed by assessment on 10 colonoscopic procedures	AccuTouch	Mixed competency scores[2]	Time to caecum[2]
Buzink *et al*[14]	35	Mixed	NRSIS	4 training sessions	GI Mentor Ⅱ	Mixed competency scores[1]	
Cohen *et al*[15]	45	Novice	MC RCT	Completion of simulator or control training programme followed by assessment of first 200 colonoscopies	GI Mentor Ⅰ	Mixed competency scores[2]	Long term impact[2]
Eversbusch *et al*[22]	28	Novice[3]	RCT	10 consecutive assessments on VR simulator	GI Mentor Ⅱ	Mixed competency scores[1]	
Gerson *et al*[24]	16	Novice	RCT	Completion of simulator or control training programme followed by assessment on 5 endoscopic procedures	AccuTouch	Mixed competency scores[2]	
Haycock *et al*[16]	36	Novice	RCT	Completion of simulator or control training programme followed by simulator and patient-based assessment	Olympus Endo TS-1	Mixed competency scores[1,2]	
Kruglikova *et al*[21]	30	Mixed	NRSIS	10 repetitions of one VR simulator task	AccuTouch	Mixed competency scores[1]	
Park *et al*[17]	24	Novice	RCT	Completion of simulator or control training programme followed by assessment on one patient-based colonoscopy	AccuTouch	Mixed competency scores[2]	
Sedlack *et al*[18]	8	Novice[3]	RCT	Completion of simulator or control training programme followed by assessment of one endoscopic procedure	AccuTouch	Mixed competency scores[2]	Patient discomfort[2]
Sugden *et al*[23]	50	Mixed	NRSIS	Completion of modules on the VR simulator	Olympus Endo TS-1	Mixed competency scores[1]	
Thomas-Gibson *et al*[19]	21	Novice	NRSIS	Completion of 5 d training programme including VR simulation, with pre- and post-training assessments followed by a 9-mo follow-up assessment	AccuTouch	Mixed competency scores[1,2]	Long term outcome (9 mo)[1,2]
Thomson *et al*[20]	13	Novice	NRSIS	Completion of respective training with or without simulator use with assessments during that period	GI Mentor	Mixed competency scores[2]	

[1]Simulator-related outcome; [2]Patient-related outcome; [3]Subjects had previous oesophagogastroduodenoscopy training and knowledge. MC: Multicentre; RCT: Randomised control trail; NRSIS: Non-randomised single-intervention study; VR: Virtual reality; GI: Gastro-intestinal.

is the only reported study to find that simulator-based training was inferior to traditional teaching methods. It concluded that simulator candidates had significantly greater difficulty with insertion of the endoscope, a lower ability to reach the splenic flexure and a lower ability for accurate retroflexion, but these findings were not replicated in other studies.

DISCUSSION

This review evaluated the evidence on the use of VR simulation endoscopy training in order to determine its role within modern educational programmes. The skill base acquired during VR simulation-supported training seems to translate into useable skills for patient-based endoscopy. In addition, learning is facilitated and skills acquisition is more effective compared to training with traditional methods alone. This applies to training in OGD (where the evidence was strongest in those who had least experience in OGD), colonoscopy and ERCP despite the small volume of literature available on this topic. There is no strong evidence for the impact of EUS VR simulator use in novice candidates when compared to traditionally trained candidates.

Integration of VR simulation in endoscopy training curricula

Our literature review did not reveal a single optimal method of integrating VR simulator use in endoscopy training programmes. This is in part due to the variety of exposures candidates had with VR simulators within each study. Whilst the majority of studies controlled candidates to a one-time formal exposure with the VR simulator[2-5,14] others allowed unlimited access[8] or optional extra-access[7,15]. The timing of this controlled exposure also varied with some being integrated

within a structured training programme[14] and some randomly during a participant's training. Despite the varied integration within the education programme, study findings were in support of VR simulator use, but further research is needed to show which approach is most effective. The main issue with the available studies is that there are significant differences in their design, in terms of sample size, candidates' prior endoscopic experience, tasks included (*e.g.,* some studies included therapeutic interventions or biopsies of specific lesions as additional tasks[2,6]), training time span, type of training (*e.g.,* some studies included hard-eye co-ordination modules, such as Endobubble/Endobasket, as well as virtual endoscopies[7,14], whereas other studies included virtual endoscopies alone[13]). These differences make comparisons between studies difficult, but there was general agreement in the literature that VR simulation training was effective in improving trainees' endoscopic skills. Therefore, despite differences in the specific interventions and differences in the endpoints of the various studies, the fact that there was an overall trend suggesting an improvement in skill level was sufficient in this review and suggests that institutions can flexibly integrate VR simulation in their endoscopy training curricula.

Optimal exposure to VR simulation

Debate still exists about the optimal exposure time needed with the VR simulator, as this was not apparent within this review. Even within those studies that controlled the exposure within a formalised teaching setting, the time which candidates had with the VR simulator varied from 5-10 h[3,5,7,22], whilst only one study stated that 20 h of exposure was needed on average to reach an expert criteria within colonoscopy[13]. However, its findings were not supported by others and more research is needed to determine the length of exposure needed with the VR simulator. There may be several explanations for the differences in the length of exposure required to achieve an improvement in performance, such as differences in the level of experience of participants, differences in simulator types, differences in the tasks (*e.g.,* some studies included therapeutic interventions or biopsies of specific lesions as additional tasks[2,6]) and collateral learning (*e.g.,* some studies included bedside teaching, educational videos or didactic modules, in addition to VR simulation practice as the main intervention[5,6,24]).

Long-term benefits of VR simulation

Whilst there was some evidence of the long-term benefits of VR simulator use when compared to traditional methods alone[3], the significance of long-term or continued training and the effect on outcomes remains unknown.

Effects of VR simulation on patient comfort

When looking at the reported discomfort or pain, only four studies found that VR simulator training reduced patients' pain significantly[13,16,18,22]. Another four studies found no significant difference between VR simulator trained and traditionally trained candidates[3,15,21,24] and only one found that patients of the VR simulator trained group reported significantly more pain[25]. More evidence is needed to show the true impact that VR simulator training has on patients' reported levels of discomfort.

LIMITATIONS

There are several issues relating to the consistency of the methodology of these studies that limits the comparison and generalisability of their findings. When looking at the studies reviewed, ten of the included studies were single-group intervention studies[2,6,8,10,12,14,19-21,23] without control groups and there were very few larger randomised control trials[15,16] (more than 30 participants). This is impacted further by the variety of different VR simulator models used, as the ability to draw accurate comparisons remains difficult.

Because of the different VR simulator models used, it is hard to accurately compare the mixed competencies used to measure candidates' skills, as measurements made in different simulator models are not truly identical. Recognition of the overall trend suggesting an improvement or reduction in skill level was sufficient in this review, negating the technicalities of the different measures.

Despite the overall trend advocating the use of VR simulators, the power of these findings is also limited by the relatively small study size. Also, as mentioned in the discussion, not all studies actively used VR simulators as part of a structured training programme and it is difficult to assess the impact of each different approach.

Finally, one limitation across all these studies was the varied definition of who was a "novice" or "experienced" candidate and the selection criteria. It was not always clear in the selection criteria how one was defined as being novice, with some studies defining a novice candidate as having no prior endoscopy experience, some as having limited experience in the procedure, whilst others allowed candidates trained in other endoscopy modalities, providing it was not the one under investigation[13,18,21]. For example, having completed less than 200 colonoscopies was defined as being a novice candidate in one study[12] whilst in the majority of studies a novice candidate had to have done no prior colonoscopies. Other studies only excluded those who had prior simulator experience[6,8]. Similarly, there were no uniform criteria among different studies regarding the definition of advanced or expert level. For example, in some studies having done more than 1000 procedures was defined as being an expert[7,13], whereas in other studies having done more than 500 procedures[8,12] or more than 30 procedures in the past 5 years[6] were considered sufficient thresholds for entering the "advanced" group. Clearly using an arbitrary number of previous endoscopies to stratify a candidate's ability and not

standardising a candidate's background experience may impact on the conclusions made in these studies.

CONCLUSION

Given the limitations of the studies, there is consistent evidence advocating the use of VR simulation in endoscopy teaching, stronger still in those who are least experienced. More evidence is needed to strengthen support of VR simulators in ERCP, as many of the models that currently exist to support this field of teaching rely on *ex-vivo* simulators not included in this review. For EUS training, more research is needed into the impact that VR simulators may have.

However, there does not appear to be a clear model in how best to integrate simulators in an educational programme. This is due to the variety of simulator models used and the lack of agreement over the length of exposure needed with any one simulator to obtain a beneficial outcome. A combined curriculum of traditional teaching supplemented with virtual reality simulators is of greater benefit than one without virtual reality simulation. Other considerations, such as the cost-benefit-analysis, although not considered here, would also influence decisions about how best to integrate VR simulators into any endoscopy curriculum.

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MINIREVIEWS

Core value of laparoscopic colorectal surgery

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Abstract

Since laparoscopy was first used in cholecystectomy in 1987, it has developed quickly and has been used in most fields of traditional surgery. People have now accepted its advantages like small incision, quick recovery, light pain, beauty and short hospital stays. In early times, there are still controversies about the application of laparoscopy in malignant tumor treatments, especially about the problems of oncology efficacy, incision implantation and operation security. However, these concerns have been fully eliminated by evidences on the basis of evidence-basis medicine. In recent years, new minimally invasive technologies are appearing continually, but they still have challenges and may increase the difficulties of radical dissection and the risks of potential complications, so they are confined to benign or early malignant tumors. The core value of the laparoscopic technique is to ensure the high quality of tumor's radical resection and less complications. On the basis of this, it is allowed to pursue more minimally invasive techniques. Since the development of laparoscopic colorectal surgery is rapid and unceasing, we have reasons to believe that laparoscopic surgery will become gold standard for colorectal surgery in the near future.

Key words: Laparoscopy; Minimally invasive surgery; Core value; Laparoscopic colorectal surgery

Core tip: This article discusses problems of oncology efficacy, incision implantation and operation security in laparoscopy on the basis of evidence-basis medicine, and also analyzes new minimally invasive technologies, their challenges and their range of application. The core value of the laparoscopic technique is studied and concluded.

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HISTORY AND CURRENT STATUS

Since 21st century, minimally invasive surgery has got revolutionary successes in more and more fields of

traditional surgery, and has become mainstream of the global surgery developments. Minimally invasive surgery has been not only the belief and pursuit of modern surgeons, but also the compulsory courses as well.

In March 1987, Franch surgeon Phillipe Mouret first used laparoscopy in cholecystectomy, which has unveiled a new era in the development of minimally invasive surgery. Compared with small incision in traditional surgery, modern minimally invasive surgery has a deeper and promoted meaning. Small incision, quick recovery, light pain, beauty, and short hospital stays are all advantages of minimally invasive surgery. People begin to realize that postoperative recovery is mainly related with abdominal incision, exposure duration and extent of damage of the abdominal cavity.

In 1990, American surgeon Jacobs completed the world's first laparoscopic right colon resection. Cutting stapling device (Endo-GIA) has greatly improved the operating conditions of laparoscopic surgery, which has made the cut-off of mesenteric vessels and bowel loops inside abdominal cavity and the lower rectal anastomosis possible. In October 1990, Dennis Fowler operated the first laparoscopic sigmoid resection using Endo-GIA. In November of the same year, Patrick Leahy completed the first laparoscopic ultra-low anterior resection (Dixon) with Endo-GIA. In July 1991, Joseph Uddo completed the first laparoscopic right colon resection. Within one year, almost all types of colon surgeries have been attempted under laparoscopy. In 1992, Kokerling completed world's first abdominoperineal resection (Miles) with laparoscopy. In our country, first laparoscopic colorectal surgery was carried out in 1993, and since then, laparoscopy was gradually used in traditional colorectal cancer surgeries. In the past 20 years, with the continuous development of laparoscopic surgical techniques and the invention and perfection of all kinds of laparoscopic equipments, laparoscopic colorectal surgery has achieved encouraging achievements, and its short and long-term effects have been approved.

With the improvement of the technologies and equipments, laparoscopic colorectal surgery is developing constantly. Mainly, laparoscopic colorectal surgery includes three techniques: Laparoscopic colorectal resection, laparoscopic assisted colorectal resection, and hand assisted laparoscopic colorectal resection. Compared with traditional open surgery, laparoscopic colorectal surgery has following advantages: (1) light postoperative pain; (2) shortened wound healing time, the abdominal incision is relatively small and beautiful; (3) faster recovery of gastrointestinal function; (4) fast-returned normal activities and short hospital stays; (5) reduced complications such as ileus, incision infection; (6) improved patient's intraoperative and postoperative immunity; (7) better operative view in narrow space such as pelvic floor; and (8) precise operation under the magnified view, which is beneficial to vascular skeletonization and lymph-node dissection.

Although laparoscopic colorectal surgery has these advantages, in early time, it did not develop fastly as people expected like laparoscopic cholecystectomy. This is mainly because of the complexity and the long "learning curve" of the laparoscopic colorectal surgery. In recent years, with the development of laparoscopic surgical techniques and the invention of ultrasound knife, Ligasure, and all kinds of intracavitary cutting stapling devices, intraoperative bleeding and operation difficulties are greatly reduced, and the operation time is also notably shortened, which has vigorously promoted the development of laparoscopic colorectal surgery. Since then, laparoscopic colorectal surgery has entered into a rapid developing stage. At present, all the colorectal cancer centers in Shanghai have carried out laparoscopic colorectal surgery, and the proportion of laparoscopic surgeries is rising year by year.

EVIDENCE OF LAPAROSCOPIC COLORECTAL CANCER SURGERY

In the early developing period, laparoscopic colorectal surgery has many controversies. This is mainly because people have a lot of concerns about the application of laparoscopic surgery in malignant tumor treatments: First, whether laparoscopic surgery may increase the incidence of implantation metastasis? And whether laparoscopic surgery can achieve radical resection? Second, whether laparoscopic colorectal surgery may increase surgical complications? Third, since in early time, the learning curve and operation time of laparoscopic colorectal surgery is obviously longer, whether laparoscopic surgery can embody minimal invasion? To answer the above questions, it is necessary to resort to evidence-based medicine for help.

Oncology efficacy

At the end of last century, a series of large randomized controlled trial (RCT) studies comparing laparoscopic and open colorectal surgeries were carried out in Europe and United States (Table 1). In 1993, Lacy *et al*[1] in Spain firstly launched RCT studies comparing laparoscopic and open colon surgeries. From then on, RCT studies such as COST in United States, COLOR in Europe, and CLASICC in United Kingdom were carried out successively[2-4], Leung *et al*[5] in Hong Kong also conducted RCT studies on laparoscopic and open colorectal surgeries. In 2002, Lacy *et al*[1] first published the result of RCT studies on short and long-term effects of laparoscopic colorectal cancer surgery. Since then, the results of RCT studies above have been completed and published one after another. The research contents involve radical resection, long-term curative effects, quality of life and cost effectiveness, *etc.*, which have provided credible clinical evidences for the application of laparoscopic colorectal cancer surgery on the basis of evidence-based medicine.

Since the lack of evidence on laparoscopic rectal

Table 1 Randomized controlled trial studies comparing laparoscopic colorectal surgery and conventional colorectal surgery

Study	No. of patients (laparoscopic *vs* conventional)	Year
Lacy *et al*[1]	219 (111 *vs* 108)	1993-1998
Leung *et al*[5]	403 (203 *vs* 200)	1993-2002
COST	872 (435 *vs* 437)	1994-2001
COLOR	1248 (627 *vs* 621)	1997-2003
CLASSIC	794 (526 *vs* 268)	1996-2002
COLOR Ⅱ	1103 (739 *vs* 364)	2004-2010

cancer surgery, Colon Cancer Laparoscopic or Open Resection Study Group in Europe launched COLORII study[6]. The study began in 2004, a total of 8 countries and 30 centers participated. From January 2004 to May 2010, a total of 1103 cases entered into the group randomly, 59 patients were ruled out for various reasons or incompleted follow-up, 1044 patients were analyzed for statistics finally. In 2013, the study reported the preliminary results. According to the results, the conversion rate of laparoscopic surgery was 17% (91/536). Compared with open surgery, laparoscopic surgery has longer operation time (240 min *vs* 188 min, $P < 0.001$), but less blood loss (200 mL *vs* 400 mL, $P < 0.0001$), faster recovery of gastrointestinal function (2 d *vs* 3 d, $P < 0.036$) and shorter postoperative hospital stays (8 d *vs* 9 d, $P < 0.036$). Postoperative pathological report shows that tumor stage, tumor size, and pathological type have no significant differences between these two groups. No significant differences were also observed in margin distance, positive margin rate and the number of lymph node dissection. The 28-d postoperative complication and mortality rates were close in these two groups. The researchers concluded that for experienced surgeons, laparoscopic rectal cancer surgery can not only meet the radical standard of open surgery, but also enhance postoperative recovery at the meantime.

Implantation metastasis problems of incision

In early times, there were controversies about whether laparoscopic colorectal cancer surgery may cause incision implantation or tumor dissemination. Once upon a time, it was reported that the rate of incision implantation was higher in laparoscopic surgery, the reason may due to the lack of standardization of the operation. In Lacy *et al*[1] study, among these 111 cases, only one had implantation metastasis in trocar puncture hole. More and more reports confirmed that as long as the surgery is operated in accordance with disease-free principles, the rate of incision implantation will not increase. After analyzing 2858 laparoscopic colon cancer cases, Stocchi *et al*[7] reported that the rate of incision implantation is only 0.7% for experienced surgeons. It was also reported, the incision implantation rate is about 0%-1.3% after laparoscopic colon cancer surgery in experienced laparoscopic centers, which has no difference with open surgery[8-11]. Standardized operation can greatly decrease the rate of incision implantation, including: (1) follow the disease-free principles during the surgery and avoid cutting tumor directly using ultrasonic knives; (2) do not stretch or squeeze tumor and simply pursue small incision when removing the tumor, take the tumor out gently with an incision protector or specimen bag, and pay attention to incision flushing at the end of surgery; and (3) before taking the Trocars out, exhaust gases from the vent hole slowly first.

Operation security problems

As the laparoscopic vision is 2-dimensional, it is often difficult to distinguish anatomical structure with spatial perception during the surgery. Moreover, laparoscopic surgery is operated by equipments, as a result, there is no hand feeling, so the laparoscopic colorectal surgery is much more difficult than ordinary laparoscopic cholecystectomy. In early time, complications of laparoscopic colorectal surgery is high, generally reported about 10%-17%. But as the advancement of "learning curve" and improvement of surgical techniques and experience, current literature reports that the incidence of complications will be gradually reduced after operating more than 30 cases. The laparoscopic peculiar complications include: Air embolism and subcutaneous emphysema, *etc*. There are also two Trocar-related complications, one is Trocar infection, but it is very rare, and does not extend hospital stays, and can be treated in outpatient clinics. The other is Trocar hernia, which is also relatively rare, and can be avoided by closing the Trocar holes carefully. Generally, laparoscopic colorectal surgery does not increase mortality, which is usually caused by systemic complications rather than the surgery itself. The life-threatened complications are extremely rare.

Arezzo *et al*[12] analysed all randomized and prospective controlled studies comparing laparoscopic and open rectal cancer surgeries in the Medline and Embase database from 2000 to 2011. Twenty-three studies including 4539 patients meet the criteria. Among them, there are 8 RCT studies, including 1746 patients. Analysis showed that within 30 d after surgery, mortality in laparoscopic group was 1.0%, while in open group was 2.4% (95%CI: 0.21-0.99, $P = 0.048$). The total complication rate was 31.8% in laparoscopic group, while 35.4% (95%CI: 0.76-0.91, $P < 0.001$) in open group. The results of meta-analysis once again prove that laparoscopic surgery has lower complications and mortality rates than open surgery.

INNOVATIVE OR CONSERVATIVE?

In recent years, new technologies in laparoscopy emerge in endlessly, including traditional laparoscopic surgery, robotic surgery, 3-D laparoscopic surgery, single-port laparoscopic surgery (SPA), natural orifice transluminal endoscopic surgery (NOTES) and transanal minimally invasive surgery (TAMIS).

We take Da Vinci Robot as an example, the system not only inherits advantages of traditional laparoscopic surgery, but has many peculiar advantages as well: (1)

there are 4 mechanical arms with the ability of 7 free degrees, which makes it possible to operate precisely in narrow and small space; (2) the thrill of hand can be filtered by computer, which improves the stability of real-time operation picture, and greatly improves the accuracy of operation; (3) high resolution 3-D image gives the operator clear and real stereo visual feedbacks; (4) the good ergonomic design allows the surgeon to operate without standing, which can significantly alleviate fatigues and is more convenient for surgeons to complete complicated and long-time surgeries; and (5) long-distance operation is possible through the robot arm controlled by remote signal transmission. However, so far, the robot's force feedback components are not perfect, because in colorectal surgery, keeping good tension is very important for the quality of operation. Moreover, robots are extremely expensive, their overall cost performance is not high enough for developing countries. So, there is still a long way to go for the popularization of robots.

3-D laparoscopic surgery has the advantages of traditional laparoscopic surgery, its high resolution 3-D image makes the operation more accurate, so it can shorten the learning curves for surgeons, especially for beginners. In order to pay more attention to minimally invasive surgery, techniques such as SPA, NOTES and TAMIS were developed in recent years, the challenges we face are how to operate safely and effectively with only one hole in the case that the surgical instruments are still deficient and how to design instruments with good handling and flexibility, these challenges decide whether these techniques would be epoch-making innovations like the birth of laparoscopy 24 years ago.

In the era of rapid development of new technologies, should a colorectal surgeon be innovative or conservative? It is hard to decide sometimes. As far as I am concerned, the key point is: the feasibility of technology does not mean the rationality of treatment. When treating colorectal cancer, the reliability of radical resection is always in the first place, the second is to minimize surgical complications, finally we may consider to operate minimally invasively. So, we should not put the cart before the horse. We should not pursue less holes and result in increasing difficulties of radical dissection and decreasing of the quality of surgery. For the new techniques like SPA, NOTES and TAMIS, they are now restricted by the existing equipments, which will undoubtedly increase the difficulties of radical dissection and the risks of potential complications. As a result, such technologies should only be confined to benign or early malignant colorectal tumors presently.

As a colorectal surgeon, we should not get lost in the tide of minimally invasive surgery and simply pursue the maximization of minimally invasion. We are delighted to see that since laparoscopic colorectal surgery was developed in China, high-resolution endoscopic vision, high levels of fine anatomy and the establishment of good training plans have made young surgeons more profound in understanding colorectal surgery, which have greatly improved the surgical quality of young surgeons. Therefore, patients are getting better quality of the surgical treatments, and gaining a better survival. Based on the above understanding, we think that the core value of the laparoscopic technique is to ensure the high quality of tumor's radical resection and less complications. On the basis of this, it is allowed to pursue more minimally invasive techniques.

After hundred years of development of colorectal cancer surgery, people's concepts have been greatly changed, the early emphasis of radical resection has been substituted by function preservation and life quality improvements on the basis of radical treatment. Minimally invasive surgery meet these requirements, which reveals the irreversible developments of laparoscopic colorectal surgery. We have reasons to believe that laparoscopic surgery will become gold standard for colorectal surgery in the near future.

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ORIGINAL ARTICLE

Observational Study

Race and colorectal cancer screening compliance among persons with a family history of cancer

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Abstract

AIM: To determine compliance to colorectal cancer (CRC) screening guidelines among persons with a family history of any type of cancer and investigate racial differences in screening compliance.

METHODS: We used the 2007 Health Information National Trends Survey and identified 1094 (27.4%)

respondents (weighted population size = 21959672) without a family history of cancer and 3138 (72.6%) respondents (weighted population size = 58201479) with a family history of cancer who were 50 years and older. We defined compliance with CRC screening as the use of fecal occult blood testing within 1 year, sigmoidoscopy within 5 years, or colonoscopy within 10 years. We compared compliance with CRC screening among those with and without a family member with a history of cancer.

RESULTS: Overall, those with a family member with cancer were more likely to be compliant with CRC screening (64.9% *vs* 55.1%; OR = 1.45; 95%CI: 1.20-1.74). The absolute increase in screening rates associated with family history of cancer was 8.2% among whites. Hispanics had lowest screening rates among those without family history of cancer 41.9% but had highest absolute increase (14.7%) in CRC screening rate when they have a family member with cancer. Blacks had the lowest absolute increase in CRC screening (5.3%) when a family member has a known history of cancer. However, the noted increase in screening rates among blacks and Hispanics when they have a family member with cancer were not higher than whites without a family history of cancer: (54.5% *vs* 58.7%; OR = 1.16; 95%CI: 0.72-1.88) for blacks and (56.7% *vs* 58.7%; OR = 1.25; 95%CI: 0.72-2.18) for Hispanics.

CONCLUSION: While adults with a family history of any cancer were more likely to be compliant with CRC screening guidelines irrespective of race/ethnicity, blacks and Hispanics with a family history of cancer were less likely to be compliant than whites without a family history. Increased burden from CRC among blacks may be related to poor uptake of screening among high-risk groups.

Key words: Colon cancer; Health disparities; Screening; Fecal blood test; Colonoscopy

Core tip: It is unclear whether suboptimal screening contributes to the increased risk of cancer within families. We evaluated compliance with colon cancer screening guidelines among adults in the United States. Our study suggested that adults with a family history of any cancer had higher screening rates, but the smallest increase was noted among blacks. Overall, screening was lower among blacks and Hispanics to such an extent that screening among those with a family member with cancer was not higher than screening among whites without a family member with cancer. There is a particular need to improve screening among high risk blacks.

Laiyemo AO, Thompson N, Williams CD, Idowu KA, Bull-Henry K, Sherif ZA, Lee EL, Brim H, Ashktorab H, Platz EA, Smoot DT. Race and colorectal cancer screening compliance among persons with a family history of cancer. *World J Gastrointest Endosc* 2015; 7(18): 1300-1305 Available from: URL: http://www.wjgnet.com/1948-5190/full/v7/i18/1300.htm DOI: http://dx.doi.org/10.4253/wjge.v7.i18.1300

INTRODUCTION

Colorectal cancer (CRC) is a leading cause of cancer-related deaths in the United States[1]. There is ample evidence that screening reduces the burden from this deadly but largely preventable disease[2-4]. Unfortunately, screening rates are suboptimal among the population, particularly among racial/ethnic minorities.

A primary driving factor for the time to initiate CRC screening is the family history of CRC[5]. However, it is well known that malignancies of other organ sites are associated with syndromic CRC such as Lynch syndrome (hereditary non-polyposis colorectal cancer)[6,7]. Lynch syndrome is caused by mutations in mismatch repair gene and is associated with an increased the risk of CRC but other malignancies such as endometrial and urogenital cancers are associated with this syndrome as well.

We hypothesized that CRC awareness should be higher among families with any history of cancer, not just CRC. This awareness should in turn be associated with uptake of CRC screening. The burden of CRC is highest among blacks due to multiple factors related to poorer access, inadequate utilization of healthcare resources even when available and possible biological susceptibility differences[8-10]. Furthermore, blacks are less likely to be aware of cancer diagnosis of their family members[11,12]. We postulated that increased CRC incidence and mortality among blacks may be due to poorer uptake of CRC screening among those at a higher risk of the disease. The aim of the present study was to evaluate compliance with CRC screening guidelines among United States adults with and without a family member with any cancer and investigate differences in compliance by race/ethnicity (whites, blacks and Hispanics).

MATERIALS AND METHODS

We used data from the 2007 Health Information National Trends Survey (HINTS) and the details of the survey have been published[13]. In summary, HINTS was a national survey of adults on health-related information and practices. It was conducted by the National Cancer Institute, National Institutes of Health in the United States between January 2008 and May 2008. The survey is available online at http://hints.cancer.gov/docs/Instruments/HINTS%202007%20CATI%20Instrument%20(English).pdf and http://hints.cancer.gov/docs/HINTS2007FinalReport.pdf.

A total of 7674 people completed the HINTS telephone interview (n = 4092), or mailed survey (n = 3582). Respondents were asked to provide information

Table 1 Comparison of characteristics of respondents with and without a family history of cancer

	Family history of cancer		*P* value
Characteristics	No	Yes	
	n = 1094 (27.4%)	*n* = 3138 (72.6%)	
Mean age, yr (95%CI)	63.4 (62.7-64.2)	63.8 (63.5-64.1)	
Sex, *n* (%)			< 0.001
Male	520 (55.8)	1158 (42.5)	
Female	574 (44.2)	1980 (57.5)	
Race, *n* (%)			< 0.001
White	818 (70.4)	2560 (82.1)	
Black	107 (12.6)	244 (9.6)	
Hispanic	92 (10.0)	134 (5.2)	
Other	62 (6.9)	123 (3.1)	
Education status, *n* (%)			0.03
Less than high school	139 (19.6)	287 (14.6)	
High school	287 (25.2)	857 (28.6)	
Some college/vocation	297 (31.1)	933 (31.7)	
College graduate	365 (24.1)	1050 (25.2)	
Marital status, *n* (%)			0.01
Unmarried	406 (32.1)	1300 (37.2)	
Married	684 (67.9)	1822 (62.8)	
Insurance status, *n* (%)			0.001
Uninsured	100 (12.1)	201 (7.3)	
Insured	983 (87.9)	2886 (92.7)	
Smoking status, *n* (%)			0.31
Never	499 (44.7)	1472 (46.2)	
Former	400 (37.4)	1205 (38.7)	
Current	179 (18.0)	419 (15.1)	
Body mass index in kg/m^2			0.82
< 25	363 (31.7)	1047 (31.7)	
25-29	406 (39.0)	1160 (37.8)	
⩾ 30	316 (29.3)	905 (30.5)	
Personal history of cancer, *n* (%)			0.06
No	908 (87.8)	2536 (85.3)	
Yes	185 (12.2)	592 (14.7)	

All percentages are weighted.

on demographic and lifestyle factors, first degree family history of any type of cancer. They were also asked about colon cancer screening with fecal occult blood test, sigmoidoscopy or colonoscopy and when they had the tests. After obtaining approval (IRB-14-MED-28) from the Institutional Review Board of Howard University in Washington DC, we downloaded the dataset. For the present study, our analytical cohort consisted of 4232 respondents (weighted population size = 80161151) who were at least 50 years old and answered questions about their family history of cancer and CRC screening compliance.

Statistical analysis

Our primary outcome was the compliance to CRC screening guidelines defined as the uptake of fecal occult blood testing within 1 year, sigmoidoscopy within 5 years, or colonoscopy within 10 years. We compared the characteristics of respondents with and without family members with a history of cancer. We used survey weights in all analyses and Taylor series linearization was used for variance estimations. Logistic regression analysis was used to estimate OR and 95%CI for the association between family history of cancer and compliance with CRC screening guidelines. We also investigated this association by race/ethnicity. Our final models included age, sex, marital status, highest education achieved, race, health insurance status, smoking status and personal history of cancer. We calculated OR and 95%CI. Statistical analysis was performed by a qualified biostatistician using Stata® statistical software version 11.2 (College Station, Texas) for all analyses. All reported percentages were weighted.

RESULTS

The comparisons of the characteristics of respondents with and without a family history of any cancer are shown in Table 1. Overall, those with a family history were more likely to be female, unmarried, and have health insurance. However, there was no difference in the prevalence of cigarette smoking, body mass index, or personal history of cancer.

When compared to respondents without a family history of cancer, those who had family members with cancer were more likely to be compliant with CRC screening (64.9% *vs* 55.1%; OR = 1.45; 95%CI: 1.20-1.74). Among whites, those with family history of

Table 2 Intra-racial comparison of being up-to-date with colorectal cancer screening by racial distribution of family history of any cancer

	Family history of any cancer	Up-to-date with CRC screening		
		Wt % screened	Unadjusted OR (95%CI)	Adjusted OR (95%CI)
Overall	No (n = 1094)	55.1	Reference	Reference
	Yes (n = 3138)	64.9	1.51 (1.25-1.81)	1.45 (1.20-1.74)
By race				
White	No (n = 818)	58.7	Reference	Reference
White	Yes (n = 2560)	66.9	1.42 (1.18-1.72)	1.49 (1.24-1.78)
Black	No (n = 107)	49.2	Reference	Reference
Black	Yes (n = 244)	54.5	1.24 (0.64-2.38)	1.34 (0.61-2.94)
Hispanic	No (n = 92)	41.9	Reference	Reference
Hispanic	Yes (n = 134)	56.7	1.81 (0.84-3.89)	1.42 (0.55-3.67)

Adjusted for age, sex, education, health insurance, BMI, smoking, marital status and personal history of cancer. CRC: Colorectal cancer; BMI: Body mass index.

Table 3 Inter-racial comparison of being up-to-date with colorectal cancer screening by racial distribution of family history of any cancer

Race	Family history of any cancer	Up-to-date with CRC screening		
		Wt % screened	Unadjusted OR (95%CI)	Adjusted OR (95%CI)
White	No (n = 818)	58.7	Reference	Reference
White	Yes (n = 2560)	66.9	1.42 (1.18-1.72)	1.45 (1.21-1.74)
Black	No (n = 107)	49.2	0.68 (0.39-1.18)	0.96 (0.51-1.80)
Black	Yes (n = 244)	54.5	0.84 (0.54-1.31)	1.16 (0.71-1.90)
Hispanic	No (n = 92)	41.9	0.51 (0.27-0.95)	0.84 (0.48-1.47)
Hispanic	Yes (n = 134)	56.7	0.92 (0.57-1.48)	1.25 (0.72-2.18)

Adjusted for age, sex, education, health insurance, BMI, smoking, marital status and personal history of cancer. CRC: Colorectal cancer; BMI: Body mass index.

cancer had 8.2% absolute higher screening rates than whites without family history of cancer (OR = 1.45; 95%CI: 1.20-1.75; Table 2). Screening rates were generally lower among Hispanics and blacks. Blacks had the lowest increase in screening rates (5.3%) when a family member had a history of cancer which was not statistically different from blacks without a family member with cancer diagnosis (OR = 1.34; 95%CI: 0.61-2.94). Although, Hispanics had the lowest screening rates among those without history of cancer (41.9%), the absolute increase in screening rates was highest among Hispanics (14.7%) when a family member has had a history of cancer.

Despite increase in CRC screening rates among blacks and Hispanics with family history of cancer, their screening rates were still numerically lower than the screening rates among whites without a family history of cancer. However, there were no statistically significant differences in the comparison of interracial screening rates (Table 3).

DISCUSSION

In the present study, we evaluated compliance with CRC screening guidelines among United States adults with and without a family history of cancer overall and by race/ethnicity. Irrespective of race/ethnicity, we found that those with a family history of cancer were more likely to be compliant with CRC screening guidelines compared to those without a family history. This pattern was present among each racial/ethnic group. However, this relationship was statistically significant only among whites. Among blacks, the absolute increase in the compliance with CRC screening among those with a family history of cancer was small. We found that screening rates were so low among blacks that the higher screening rates observed among blacks with family history of cancer were still numerically lower albeit not statistically different from the screening rate among whites without a family history of cancer. This suggests that the increased CRC burden among blacks may be, in part, due to low screening rates among high risk blacks and underscores the need to increase awareness and screening rates among blacks.

Although the Hispanics in this study have the lowest CRC screening rates among those without a family history of cancer, they exhibited the highest absolute increase in CRC screening among those with a family history of cancer. This suggests an appropriate response in uptake of preventive services among Hispanics, but the screening rates were still lower than that among whites without a family history of cancer. This finding indicates that increased education about CRC screening is needed among Hispanics.

We are not aware of any other study that has examined the association of a family history of any

cancer with CRC screening for a direct comparison to our study. However, prior studies have examined the CRC screening among persons with a family history of CRC. Using data from the 2005 California Health Interview Survey (CHIS), Ponce *et al*[14] reported that screening rates were lower among Hispanics in general when compared with whites, but disparities were more pronounced among respondents with a family history of CRC (OR = 0.28; 95%CI: 0.11-0.60) as compared to disparity among those without family history of CRC (OR = 0.74; 95%CI: 0.59-0.92). However, CRC screening rate was comparable among blacks and whites among those with (OR = 0.92; 95%CI: 0.31-1.34) or without a family history of CRC (OR = 1.08; 95%CI: 0.84-1.40). In another study which used the 2009 CHIS, Almario *et al*[15] investigated CRC screening among respondents with a family history of CRC in California. The authors reported that there was no difference in overall screening rate among blacks when compared to whites (OR = 1.03; 95%CI: 0.81-1.27). However, among individuals who were 40-49 years old (when early screening should have started because of the increased risk of CRC), blacks were 71% less likely to have had a colonoscopy (OR = 0.29; 95%CI: 0.04-0.87). Taken together, these two studies suggest lower rates of appropriate CRC screening among blacks and Hispanics at an increased risk of CRC. However, the studies focused only on residents of the state of California. Nonetheless, these findings were comparable to our findings that are based on nationally representative data of United States adults.

It is unclear why the rates of CRC screening was lower among these minority populations, but we speculate that known factors such as health literacy, access and utilization differences may be playing important roles. In a previous study using the 2007 HINTS data, Orom *et al*[16] reported differences in perceived cancer risk by race. The authors reported that Hispanics were less likely to perceive themselves at higher risk of cancer even when they have family members with cancer. This disconnect may be related to health literacy or communication challenges. It is well known that blacks are less likely to discuss their chronic health problems with family members[17,18] and often hold fatalistic beliefs which negatively correlate with uptake of preventive services such as CRC screening[19].

There are some notable strengths of our study. We examined compliance with CRC screening guidelines among a nationally representative large sample of United States adults and two modes of survey was used (mail and telephone), thereby increasing the reach of the survey. Furthermore, the survey was conducted in English and Spanish to ensure broader participation. However, our study has important limitations. Although we do not suspect that respondents would have any motivation not to tell the truth, but our study was based on self reports and we could not abstract medical records to verify CRC screening uptake and the time they took place. Also, the race designation in the HINTS survey was by self-identification. Furthermore, our study did not capture other factors which may influence CRC screening compliance such as accessibility to healthcare facilities, availability of culturally sensitive care providers and type of health insurance coverage.

In conclusion, while being up-to-date with CRC screening is generally higher among those with a family history of cancer, blacks and Hispanics with a family history of cancer were less likely to be compliant with CRC screening guidelines compared with whites without a family history of cancer. There is a need to improve cancer education among blacks and Hispanics and increase CRC screening rates, especially among higher risk groups.

COMMENTS

Background

The risk of cancer is higher among families when a member has been diagnosed with cancer. The current study evaluated compliance with colorectal cancer (CRC) screening guidelines among adults with and without a family member with a history of cancer.

Research frontiers

The CRC screening rates were higher among United States adults with family members with cancer diagnosis. By race, CRC screening rates among blacks and Hispanics were lower than whites. The screening rates among blacks and Hispanics with family history of cancer did not even reach the level of screening among whites without family history of cancer.

Innovations and breakthroughs

The current study examined whether United States adults with a family history of cancer were more likely to be compliant with CRC screening guidelines. This has not been thoroughly investigated previously.

Applications

Blacks and Hispanics have lower screening rates than whites even when they have family members with history of cancer. This study suggests that the low absolute increase in CRC screening rates among blacks when a family member has a history of cancer may represent inadequate CRC screening uptake among high risk blacks. This may be playing a role in the observed CRC disparity by race in the United States.

Terminology

Screening for CRC reduces the incidence and mortality from the disease.

Peer-review

The manuscript is a well-designed observational study that addressed a major issue about health behavior among different races. The authors managed to reveal this issue through extensive research and thorough statistical analysis.

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