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REVIEW

Endoscopic ultrasound guided liver biopsy: Recent evidence

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Abstract

Liver biopsy (LB) is an essential tool in diagnosing, evaluating and managing various diseases of the liver. As such, histopathological results are critical as they establish or aid in diagnosis, provide information on prognosis, and guide the appropriate selection of medical therapy for patients. Indications for LB include evaluation of persistent elevation of liver chemistries of unclear etiology, diagnosis of chronic liver diseases such as Wilson's disease, autoimmune hepatitis, small duct primary sclerosing cholangitis, work up of fever of unknown origin, amyloidosis and more. Traditionally, methods of acquiring liver tissue have included percutaneous LB (PCLB), transjugular LB (TJLB) or biopsy taken surgically via laparotomy or laparoscopy. However, traditional methods of LB may be inferior to newer methods. Additionally, PCLB and TJLB carry higher risks of adverse events and complications. More recently, endoscopic ultrasound guided LB (EUS-LB) has evolved as an alternative method of tissue sampling that has proven to be safe and effective, with limited adverse events. Compared to PC and TJ routes, EUS-LB may also have a greater diagnostic yield of tissue, be superior for a targeted approach of focal lesions, provide higher quality images and allow for greater patient comfort. These advantages have contributed to the increased use of EUS-LB as a technique for obtaining liver tissue. Herein, we provide a review of the recent evidence of EUS-LB for liver disease.

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Core tip: Endoscopic ultrasound guided liver biopsy is a safe and effective approach to obtaining liver biopsies that may serve as an alternative to traditional methods. Our goal is to collect and review the most recent data on the advances in endoscopic ultrasound guided liver biopsies, while also weighing the advantages and disadvantages of utilizing conventional methods of liver biopsy (percutaneous liver biopsy, transjugular liver biopsy, surgical liver biopsy).

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INTRODUCTION

Needle biopsy of the liver was first performed by Dr. Paul Ehrlich in 1883[1]. Since then, the role and technique of tissue sampling has evolved tremendously. Liver biopsy (LB) provides essential clinical information regarding diagnosis, prognosis, evaluation and management of various diseases of the liver[2]. Though patient history, clinical exam, imaging and laboratory tests including serology aid in the initial diagnosis of liver disorders, histological analysis continues to play an essential role in discovering the etiology and magnitude of liver disease, especially when preliminary, less invasive methods of evaluation are inconclusive[3]. Without tissue acquisition, nearly one-third of cases of liver cirrhosis can be overlooked in patients presenting with abnormal liver tests and absent diagnostic serology, though the widespread availability and non-invasive nature of fibro -elastography has helped reduce the need for biopsies[4].

There are several approaches available to acquire a LB. Conventionally, LBs have primarily been performed through the computed tomography (CT) or ultrasound (US) guided percutaneous (PC) route[1]. In cases in which this approach is contraindicated or unavailable, a fluoroscopy guided transjugular (TJ) approach may be employed, which may be combined with measurement of hemodynamics in the portal system[5,6]. Less commonly, a surgeon may perform a LB during laparoscopy/laparotomy[2]. However, there are procedure-related risks including mortality related to traditional methods of acquiring liver tissue. Major complications following LB are rare, occurring at a rate of approximately 1%, while mortality rates occur at 0.2%[7]. The most common complications include hemorrhage and pain[8,9]. Further, the use of PCLB and TJLB may have substantial variation in histologic yield[10].

Endoscopic US guided LB (EUS-LB) is a sampling technique that has surfaced as an effective alternative to traditional methods of obtaining liver tissue both for focal and parenchymal disease[11]. In addition to an improved safety profile, EUS-LB presents numerous advantages over PC and TJ routes of biopsy. Briefly, EUS-LB allows for higher quality images of both hepatic lobes, which allows for a safer biopsy technique and improved ability to access focal liver lesions[12]. Additionally, EUS-LB is conducted under sedation, allowing for reduced procedural anxiety and increased patient comfort[13]. Ultimately, the decision on the route of tissue acquisition largely relies upon the indications for the LB, the patient risk profile and the experience of the endoscopist, including the procedural volumes.

Given the superiority of EUS-LB in various aspects, this article aims to provide an update on the emerging evidence, indications, technique, advantages, and complications. This will ultimately help physicians determine the most appropriate method of LB.

INDICATIONS FOR LB

The use of imaging, including newer modalities like transient elastography and serology, has helped decrease the need for LBs. For instance, in a patient with established cirrhosis, a solid liver lesion with certain characteristics on magnetic resonance imaging and compatible tumor markers, the diagnosis is presumably hepatocellular carcinoma and would not necessarily require a LB[14]. Similarly, in cases in which a liver lesion is most likely related to metastasis from a proven primary cancer, biopsy may not be indicated unless there is enough evidence to the contrary or tissue is needed for diagnostic confirmation or workup for specialized molecular tests[14].

However, there are several clinical scenarios that warrant LB. One of the most common utilities of LB is diagnosing the etiology of complex liver disease that cannot be reasonably identified by imaging, serology or laboratory values[14]. LB can also useful in distinguishing cases where there are disease processes that overlap such as in autoimmune hepatitis and drug induced liver injury[15]. Additionally, LBs are essential to establishing a diagnosis and staging of diseases such as nonalcoholic steatohepatitis (NASH), chronic liver disease due to hepatitis B and C, autoimmune hepatitis, and acute liver failure of indeterminate etiology, amongst other liver diseases[16]. LB can also help diagnose systemic diseases, such as amyloidosis and sarcoidosis, that can affect the liver and assist in the work up of pyrexia of unknown origin[1,16].

LBs can be crucial to assessing disease severity and establishing prognosis. While serology is useful to establish a diagnosis of viral hepatitis, the LB helps to quantify the extent of inflammation or fibrosis, as well as identification of concomitant disease processes, which may have significant prognostic implications[16]. Similarly, in hemochromatosis, the presence of fibrosis can predict the risk of transformation to hepatocellular carcinoma[16,17]. Transient elastography techniques have decreased the need for LB in deciding on treatment options in many conditions like chronic viral hepatitis. With the availability of directly acting antivirals for treatment of chronic hepatitis C infection, fibrosis staging is most of the time performed using transient elastography. But in chronic viral hepatitis and many other hepatitis diseases like auotoimmune hepatitits, alcoholic and non alcoholic steatohepatitis, assessment of grade of activity can be accomplished only by LB. Distinguising some of the rare conditions like nodular regenerative hyperplasis from cirrhosis can be accomplished only with LB[2,16].

METHODS OF LB

The methods of LB are mainly categorized into three groups including traditional methods, surgical based, and EUS-guided approaches. Each method has its own pros and cons as summarized in Table 1.

Traditional methods of acquiring LB

PCLB: The earliest known PC biopsy of the liver was conducted in the early 1900s and has since remained the primary method of sampling liver tissue[18]. In the PCLB method, a biopsy site is pinpointed over the liver, an incision is made in the skin aseptically under local anesthesia, and a needle is inserted into the liver to obtain a tissue sample[19]. In its infancy, the PCLB was performed without image guidance from the right lobe of the liver and was identified by percussion of the liver, with breath held in inspiration[20]. However, this is now performed under CT or ultrasonographic guidance, minimizing adverse events[21]. Early operators commonly used a 14 or 16-gauge (G) needle to obtain a core biopsy specimen. However, most operators now utilize 16-18G needles to obtain biopsy[22,23].

While use of CT or US guided biopsy has helped to decrease inadvertent punctures of adjacent organs, complications still occur[24]. The most common complication is hemorrhage[22]. Minor complications occur in nearly a quarter of cases, the most common being pain at the site of biopsy[25]. Other reported complications include peritonitis[26], hypotension[27], infection, gallbladder perforation[28], pneumothorax or hemothorax[29], transient bacteremia[30] and mortality[7,31].

Advantages/disadvantages of PCLB: One of the advantages to employing the PCLB method is that operators are more familiar with this method and have a better understanding of this technique and of the specimen. Thus, compared to newer methods, this is comparatively easier to use and demands less technical skill[11]. Additionally, the PCLB route is cost effective, allowing for widespread use in various clinical settings.

Table 1 Advantages and disadvantages of liver biopsy methods

	Percutaneous liver biopsy	Transjugular liver bipsy	Surgery	Endoscopic ultrasound guided liver biopsy
Indication	Mainstay method of liver biopsy for unexplained abnormal LFTs, assessing, staging, diagnosing liver disease	Coagulopathy; ascites; morbid obesity; failure of percutaneous liver biopsy ; thrombocytopenia	Undergoing surgery for another indication	Undergoing endoscopy for another indication
Complications	Pain; hemorrhage; peritonitis; hypotension; infection; gallbladder perforation; pneumothorax; hemothorax	Hemorrhage; pain capsule perforation; arterial aneurysms; arrhythmias	Hemorrhage, abdominal wall injury; intraperitoneal injury; anesthesia related complications	Hemorrhage; abdominal pain; infection
Advantage	Well-known procedure; cost effective; less technical skills required	Decreased risk of complications; more tolerable; useful in patients with comorbidities	Can take LB while performing another procedure	Increased tolerability; decreased recovery time; decreased complications; bi-lobar access; decreased sampling variability; View anatomical/vascular structures
Disadvantage	Increased sampling variability; less tolerable; require more passes; increased risk of complications	Limited view of liver parenchyma and vascular anatomy; increased sample fragmentation	Invasive; requires surgical specialty	Costly, if not performed along with another endoscopic procedure

While the PC route is cost effective and well-known, several disadvantages exist[2]. There is increased likelihood of sampling variability. Patients experience more discomfort at the puncture site, which could at times last for weeks, as the needle traverses multiple layers to access the liver and could potentially injure the intercostal nerves and vessels. Additionally, lower image resolution, higher post procedure recovery time and higher risk of complications are also disadvantages to this technique[32]. Lastly, compared to other methods, the PC method typically requires more passes to acquire an adequate tissue sample, thus increasing the risk of complications and the level of discomfort[32,33].

TJLB: Liver tissue can also be sampled *via* a TJ route, which was introduced in 1964 by Dotter[34]. In this method, an interventional radiologist introduces a guidewire into the jugular vein (commonly the right JV), followed by a needle sheath, and advanced down into the hepatic veins via the inferior vena cava, to measure portal hemodynamics and to sample the liver, circumventing the liver capsule and peritoneum. A smaller 18 or 19 G fine-needle aspiration (FNA) needle is currently being used[34,35].

This method is typically reserved for patients who have a coagulopathy, need measurement of portal pressures and gradients, are morbidly obese, or have significant ascites[1,19,36]. In patients with acute liver failure of indeterminate etiology where metastatic liver infiltration is suspected, alcoholic hepatitis, or abnormal liver tests in patients who are bone marrow transplant recipients, this method is preferable[37,38].

Complications following TJ LB are rare, 2.5%-7.1%[36,39]. A retrospective study (n = 601) by Mammen *et al*[39] of patients who had undergone TJLB reported a 2.5% complication rate. Kalambokis *et al*[5] also conducted a large systematic review (7649 TJLBs) on TJLB and found an overall complication rate of 7.1%. Major complications following TJLB include pain and hemorrhage[36]. An inherent risk of this method includes complications related to placement of the jugular catheter[16]. Other complications include inadequate sample size, hepatic hematoma, pyrexia, arrhythmias, abdominal pain, pneumo-thorax, haemobilia, carotid puncture, hypotension, capsular perforation, hepatic portal vein fistula and hepatic artery aneurysm[5].

Advantages/disadvantages of TJLB: One of the main advantages to this method is the decreased risk of overall complications compared to PCLB, even with multiple passes[32]. Given that the TJLB method avoids the liver capsule, there is little risk of causing injury to Glisson capsule and subsequent pain. As such, patients report increased tolerability and less pain. Secondly, this allows for decreased use of analgesia for pain control[2,32] .

Other advantages to the TJLB is its ability to be used in patients who have contraindications to PCLB. For example, this allows for assessment of liver disease in

patients with coagulopathy and acute liver failure[40]. This approach can also be utilized for dual purpose in patients with cirrhosis who require multiple interventions such as measurement of hepatic venous pressure and transjugular intrahepatic portosystemic shunt placement in addition to obtaining tissue sample[41].

The TJLB method, however, is limited in its ability to view the liver parenchyma and vascular anatomy on ultrasound. Another disadvantage of TJLB is that samples obtained have typically been more fragmented and smaller in size compared to PCLB, making pathologic evaluation at times inconclusive[1,42].

Laparoscopy/laparotomy

Laparoscopy or laparotomy represents another option for hepatic tissue acquisition that is typically used when a patient is already undergoing surgery for another indication and gross liver abnormalities are noted[43]. LBs undertaken with this approach are mostly done by wedge resection or cutting/aspiration needle. It is most useful in targeted biopsies of liver masses, staging tumors and in patients found to have inconclusive results using the PCLB or TJLB method[2].

Complications: Adverse events following the surgical approach to LB include hemorrhage, abdominal wall injury, intraperitoneal injury and those related to use of anesthesia[2].

Advantages/disadvantages: One advantage to the surgical approach to LB is that it allows for ample tissue collection, and has an extremely high diagnostic tissue yield[43]. In a retrospective study of laparoscopic LBs by Vargas *et al*[44], a conclusive diagnosis of cirrhosis was made in 93 percent of 1794 cases. Additionally, the surgical approach allows for evaluation of the gross features of the liver, as well as other important peritoneal structures. Studies have shown that the added ability to grossly evaluate the liver allows for detection of up to 30% more cases of liver cirrhosis than with LB alone[45]. Operators can also coagulate puncture sites immediately in the event of bile leakage or overt hemorrhage, which allows for LB in patients with higher risks of bleeding[46].

A disadvantage to the surgical approach is that surgery is more invasive, hence limiting its use to patients who require surgery for some other indication. A laparoscopic LB can also be more expensive, further limiting its widespread routine use[2].

EUS-LB

EUS, developed in the late 1980s and refined in the 1990s, represents a more recent approach to acquiring hepatic tissue for histological analysis[47-49]. Ever since the availability of core biopsy needles, they have been used exclusively for EUS-LB, rather than conventional fine needles. The latter is currently utilized when cytology is sufficient and tissue architecture is not critical to diagnosis. In this approach, the left lobe of the liver is identified by the echo-endoscope from the stomach and the right lobe (Figure 1) from the duodenal bulb. With use of color doppler imaging, proper care is taken to ensure there are no vascular structures along the needle path[19]. Commonly, a 19-G core biopsy needle is used to sample the left lobe followed by the right lobe[2].

Adverse events/complications: EUS-LB is generally safe, with few adverse events reported in the literature (Table 2). In a meta-analysis of studies (n = 437) reporting on EUS-LB, the rate of adverse events was 2.3%, with minor bleeding as the primary complication[50]. Additionally, Diehl *et al*[51] conducted a multicenter, prospective study (n = 110) on the diagnostic yield and safety of EUS-LB done for evaluation of abnormal liver enzymes. Out of 110 participants, one patient who had a medical history of coagulopathy and thrombocytopenia developed a non-active pericapsular hematoma that was managed conservatively[51]. Adler *et al*[52], Mok *et al*[53], Gleeson *et al*[54] and Stavropoulos *et al*[55] have conducted similar studies (n = 200, 40, 9 and 22, respectively) regarding EUS-LB with a 0% rate of complications.

Advantages of EUS-LB: There are several advantages to utilizing the EUS-LB technique over more conventional methods of acquiring tissue samples. Generally, the EUS-LB is less invasive compared to the surgical/transjugular routes, translating to lower patient and procedure related adverse events. The EUS-LB provides clinicians with a real-time, detailed view of the biopsy needle through the course of the liver and the trajectory can be changed if needed as part of the "fanning" technique to get a more representative sample[11,56] (Figure 1). Multiple cores can be obtained if needed, without increasing patient discomfort, though traditionally we take one core each from the right and left lobes. This ultimately helps to better identify and avoid important anatomic structures (intrahepatic vessels, major bile duct, *etc*.)

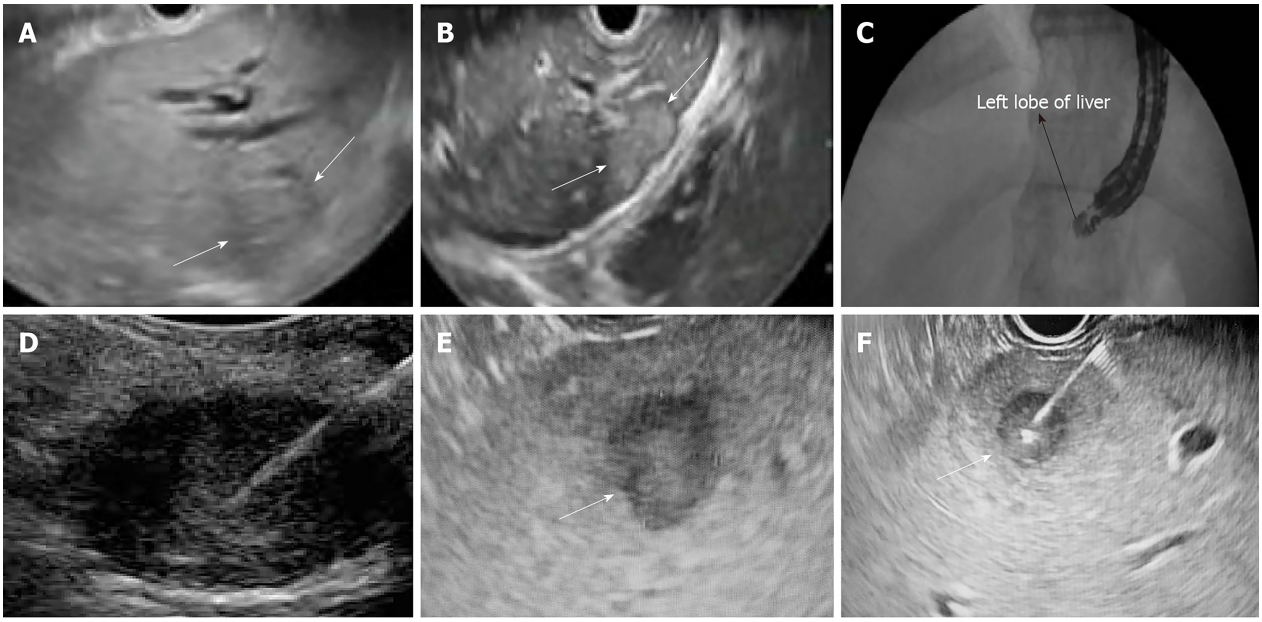

Figure 1 The endoscopic ultrasound guided liver biopsy provides clinicians with a real-time, detailed view of the biopsy needle through the course of the liver.

due to the proximity of the ultrasound device to the liver[56,57]. Whereas the PC and TJ methods have limited access to sample different areas of the liver, the EUS method allows greater access to both hepatic lobes, increasing the adequacy and yield of tissue[55,58]. Additionally, EUS allows for detection of smaller hepatic lesions and retroperitoneal structures (*i.e.*, lymph nodes) and sampling of neighboring organs that are occasionally missed by CT scan[59,60].

Patients also benefit from EUS-LB. Given that the anticipation and uncertainty of procedures may provoke anxiety in patients, EUS-LB is performed with either conscious sedation or under anesthesia, improving patient tolerance[61]. The procedure is quick, adding only a few minutes to the overall procedure time as shown by Diehl *et al*[13]. Post procedural discomfort is significantly lower in our experience in comparison to PC. Additionally, compared to conventional LB methods, EUS-LB has an average recovery time of four hours compared to ten hours in the PC method[62,63]. Patients are normally observed in the recovery room for 30 min as for any other EUS biopsy unlike 4 h for PCLB, which allows for rapid patient turnover and increased efficiency[13]. EUS-LB would also be suitable for individuals who are obese and may not be appropriate for the PCLB approach as well as for those who refuse the latter. Lastly, for patients who are planning to undergo an endoscopic procedure for another medical indication (*e.g.* screening for Barrett's, gastroesophageal reflux disease, varices or esophagogastroduodenoscopy done as part of evaluation of dyspepsia) a LB can be performed simultaneously if required under the same anesthesia, reducing time, cost and risk of multiple procedures just for tissue acquisition.

Disadvantages of EUS-LB: While EUS-LB has favorable components compared to earlier techniques, there are some disadvantages associated with its use. First, EUS-LB is a relatively new technique. As such, many clinicians who have grown accustomed to obtaining liver samples via the PC or TJ route have less experience utilizing this method[50]. Similarly, the process of learning to use traditional methods of LB is much simpler compared to the higher level of technical skills required to learn and utilize the EUS-LB[64]. The core biopsy, though it often meets the criteria proposed by international societies (as mentioned in Table 3), will be smaller, as the needle commonly used is a 19G fine needle biopsy (FNB) for EUS, compared to a 16G in the PCLB route. Additionally, undergoing endoscopy for the sole purpose of LB can be expensive, therefore limiting widespread utilization[19].

COMPARISON OF THE ADEQUACY OF DIAGNOSTIC SAMPLES AMONG LB METHODS

Obtaining an adequate histological sample is a vital step in the process of establishing a diagnosis. Various authorities have attempted to create objective parameters to

Table 2 Comprehensive review of studies on endoscopic ultrasound guided liver biopsy

Ref.	Study design	*n*	Indication	Needle used	No of passes	CPTs	TSL	Insufficient sample	Adverse events
Wiersema *et al*[70], 2002	Prospective cohort	9	No medical indication	19G Tru-cut	NR	1	4 mm	0	None
Gleeson *et al*[54], 2008	Retrospective case series	9	Hepatic parenchymal disease	19G Tru-cut	2	7	16.9 mm	0	None
DeWitt *et al*[71], 2009	Prospective case series	21	Hepatic parenchymal disease	19G Tru-cut	3	2	9 mm	10%	None
Stavropoulos *et al*[55], 2012	Prospective case series	22	Abnormal LFTs	19G FNA (non-Tru-cut)	2	9	36.9 mm	9%	None
Gor *et al*[73], 2014	Prospective case series	10	Abnormal LFTs; Suspected cirrhosis	19G FNA (non-Tru-cut)	3	9.2	14.4 mm	0	None
Diehl *et al*[51], 2015	Retrospective cohort	110	Persistent transaminitis	19G FNA Expect Flexible	1 to 2	14	38 mm	2%	Self-limited bleeding
Lee *et al*[67], 2015	Prospective cohort	21	Rescue for PCLB	22G FNB, 25G FNB	2	NR	NR	9.50%	None
Pineda *et al*[66], 2016	Retrospective cohort	110	Abnormal LFTs of Unknown Etiology	19G FNA Expect/Flexible	3	14	38 mm	2%	NR
Sey *et al*[72], 2016	Prospective Cross-sectional	75	Suspected parenchymal disease	19G FNB ProCore; 19G FNB Tru-Cut	2; 3	5; 2	20 mm; 9 mm	3%; 27%	None; Pain
Schulman *et al*[79], 2017	Prospective ex-vivo	48	No medical indication	18G1 (percutaneous); 18G2 (percutaneous); 19G FNA Expect; 19G FNB ProCore; 19G FNB SharkCore; 22G FNB SharkCore	1 to 2	2.5; 3.5; 1.9; 1.7; 6.2; 3.8	NR; NR; NR; NR; NR; NR	16.7%; 18.7%; 54%; 81%; 14.6%; 14.6%	None
Mok *et al*[53], 2017	Prospective cross-over	20	Elevated LFT Unknown Etiology	19G FNB; 22G FNB SharkCore	NR	7.4; 6.1	76.5 mm; 66.9 mm	2.5%; 2.5%	None; Pain
Shah *et al*[75], 2017	Retrospective chart review	24	Abnormal LFTs, pancreaticobiliary disease	19G FNB SharkCore	2	32.5	65.6 mm	4%	Pain; Subcapsular bleeding
Saab *et al*[87], 2017	Retrospective chart review	47	Biliary tract disease, abnormal LFTs	19G FNB SharkCore	NR	18	65 mm	0	Self-limited liver; hematomas
Ching-Companioni *et al*[83], 2018	Prospective randomized	40	Abnormal LFTs	19G FNA Expect Flexible; 19G FNB Acquire	1; 1	38; 16.5	11.8 mm; 16.3 mm	0	Pain
Nieto *et al*[76], 2018	Prospective observational	165	Unexplained abnormal LFTs, biliary obstruction	19G FNB SharkCore	1	18	60 mm	0	Abdominal pain; Self-limited hematoma
Mok *et al*[80], 2018	Prospective cross-over	40	Parenchymal liver disease	19G FNA Expect Flexible; 19G FNA Expect Flexible; 19G FNA Expect Flexible	3	4; 4; 7	23.9 mm; 29.7 mm; 49.2 mm	20%; 7%; 2%	Postprocedural bleeding

Rombaoa *et al*[69], 2018	Retrospective chart review	8	Unexplained abnormal LFTs, hepatitis B staging, cirrhosis	19G FNB Acquire	2	9.4	NR	NR	None
Shuja *et al*[68], 2019	Retrospective observational cohort	69	NASH fibrosis staging	19G FNA Expect Flexible	3	10.84	45.8 mm	NR	None
Hasan *et al*[77], 2019	Prospective nonrando-mized trial	40	Elevated liver enzymes	22G FNB Acquire	2 L; 1 R	42	55 mm	0	Self-limiting abdominal pain
Bazerbachi *et al*[78], 2019	Prospective cohort	41	NAFLD diagnosis, staging	22G FNB Fork-tip	2	26	24 mm	0	Postproce-dural pain

FNB: Fine needle biopsy; FNA; Fine needle aspiration; TSL; Total Specimen length; CPT: Complete portal tracts; *n*: Number of study participants; NAFLD: Non-alcoholic fatty liver disease; NASH: Nonalcoholic steatohepatitis.

assess the adequacy of samples, with very little consensus (Table 3). Adequacy has largely been described by the length of total specimen (TSL) and/or number of complete portal triads (CPTs), which includes the portal vein, hepatic artery and bile duct[65]. Occasionally, the length of the longest piece (LLP) of tissue is also included as a defining element. Nonetheless, few studies have directly compared the adequacy of histologic samples acquired through conventional and novel methods of LB.

Pineda *et al*[66] conducted a retrospective study comparing the adequacy of LB tissue samples obtained through the PCLB, TJLB and EUS-LB methods. PCLB was obtained with spring-loaded 18G, 19G, or 20G needles. TJLB samples were obtained with 18G or 19G needles and EUS-LB samples were obtained with regular 19G FNA needles. The number of CPTs and TSL using the EUS-LB method was found to be equivalent to PCLB and TJLB when only the left lobe was sampled. However, the study found that CPTs and TSL were significantly higher through the use of EUS-LB when both lobes were biopsied[66]. Similarly, a 2015 study (n = 21) by Lee *et al*[67] found that EUS-FNB could deliver adequate tissue samples and serve as an effective rescue method of LB in patients in which the PCLB method failed to obtain adequate tissue or render a diagnosis. Shuja *et al*[68] also retrospectively (n = 152) compared the adequacy of biopsies using the EUS-LB, PCLB, and TJLB methods for staging NASH fibrosis and found that EUS-LB produced increased TSL compared to traditional methods, with fewer complications. Likewise, Rombaoa *et al*[69] conducted a 2018 retrospective study (n = 8) of patients who had undergone EUS-LB with a 19G Acquire needle for abnormal LFTs, hepatitis B staging and cirrhosis. In the same study, they compared procedural and specimen results of patients who had a biopsy with the PCLB and EUS-LB method and found that numbers of CPTs were similar for both, but length of procedure and recovery times were much lower for patients in the EUS-LB group[69]. As it seems, EUS-LB is comparable to conventional methods, while improving safety profile and providing a more efficient method of obtaining liver tissue. Figure 2 demonstrate the histology of LB from the EUS approach.

EUS-LB: Early Tru-Cut needle

Early studies evaluating the efficacy of EUS-LB describe initial experiences using the 19G Tru-cut needle, albeit with variable outcomes. In a 2002 study, Wiersema *et al*[70] described EUS-LB using a 19G Tru-Cut needle in swine models that produced a median TSL of 4 mm with 100% procurement of core tissue samples. However, the authors in this study reported procedural difficulty due to the rigidity and inflexibility of the needle while going through the endoscope[70]. Later, Gleeson *et al*[54] conducted a case series review of nine patients who had undergone EUS-LB with the 19G Tru-cut needle for a variety of indications (*i.e.*, dilated CBD, abnormal liver tests with suspicious image findings and tumor staging). The mean TSL was 16.9 mm, median number of CPTs was seven, and adequate diagnostic material was acquired in 100% of cases[54]. However, in a 2009 study by DeWitt *et al*[71], 21 patients were evaluated for benign liver disease with the same Tru-Cut biopsy needle. A histologic diagnosis was obtained in 90% of cases, but the size of the samples did not meet standard criteria for histologic assessment[71]. The Tru-Cut needle, partially due to the inflexible design, was deemed difficult to use, limiting its widespread adoption.

EUS-LB with FNA

Given the limited adoption of the early TruCut needle, the search for alternative EUS-LB needles led to the use of a 19G EUS–FNA needle, which has long served as the

Table 3 Summary of society guidelines for adequate liver biopsy

Medical society	Total specimen length	Complete portal triads	Needle size
American Association for the Study of Liver Diseases	2-3 cm	≥ 11	16G
European Association for the Study of the Liver	15 mm	-	-
Asian Pacific Association for the Study of the Liver	15 mm	≥ 10	16G

mainstay for obtaining hepatic tissue. Multiple studies have demonstrated the accuracy and practicality of EUS-FNA using the 19G needle[71-73]. In 2012, Stavropoulos *et al*[55] conducted a prospective case series of EUS-LB with a regular non-Tru-cut 19-G FNA needle in 22 patients with abnormal LFTs of unclear etiology. With a median TSL of 36.9 mm, median of 9 CPTs and a diagnosis achieved in 91% of cases, the authors concluded that EUS-FNA with a 19G FNA needle was effective with good diagnostic yield[55]. Later, in a 2014 study (n = 10) by Gor *et al*[73], patients had an EUS-LB with a 19G FNA needle for abnormal LFTs. There was a yield of 100% diagnostic adequacy, a mean TSL of 14.4, and a mean CPT of 9.2 with no reported complications[73]. In 2015, Diehl *et al*[51] presented a large multicenter study (n = 110) in patients with elevated liver enzymes who had an EUS-LB with a 19G FNA needle. The median TSL was 38 mm, with a median of 14 CPTs, yielding adequate tissue for diagnosis in 98% of the cases. Adverse events were uncommon, but bleeding was reported in one patient with a history of coagulopathy[51]. Though widely implemented, EUS-FNA may be limited in its ability to provide core tissue samples with good architecture. Further, the diagnostic yield of FNA is variable, depending on needle the size and type, operator experience as well as the obtainability of rapid onsite evaluation (ROSE).

EUS-LB with FNB

The increasing utility of EUS-FNB, partly due to the advent of newly designed, more flexible, biopsy needles (EchoTip, ProCore, SharkCore, Acquire needle, EZ shot 3 plus needle, *etc*.) may improve diagnostic yield of LBs, and reduce or possibly negate the need for ROSE[74].

In a 2016 cross-sectional study (n = 75) Sey *et al*[72] compared the diagnostic yield of a novel reverse bevel 19G FNB ProCore needle with the early 19G Tru-cut biopsy needle. The authors found that EUS-LB with the newer ProCore needle produced specimens with a longer median length (20 mm *vs* 9 mm), more CPTs and more adequate specimens with fewer passes. Shah *et al*[75] reached a similar conclusion in a retrospective study (n = 24) of patients with abnormal LFTs and pancreatobiliary conditions, who had undergone EUS-LB with a novel 19G FNB SharkCore. A histologic diagnosis was achieved in 96% of cases, with a median TSL of 65.6, median CPT of 32.5 and a median of two passes. Nieto *et al*[76] conducted a recent 2018 retrospective study (n = 165) using a modified 1-pass wet suction technique in patients with elevated LFTs of unclear etiology who had undergone EUS-LB for exclusion of biliary obstruction. The median TSL in their study was 6 cm, the median number of CPTs was 18 and the authors concluded that EUS-LB with the modified 1-pass wet suction technique was safe and effective.

Recent studies have also demonstrated potential use with a smaller, 22G FNB needle. In a 2019 study (n = 40), Hasan *et al*[77] analyzed biopsy results of patients referred for evaluation of elevated LFTs. There were two passes made from each hepatic lobe, yielding a median TSL of 55 mm, a median CPT of 42, and 100% specimen adequacy. Self-limiting abdominal pain was the only complication reported. In another recent 2019 prospective study (n = 41), Bazerbachi *et al*[78] demonstrated that EUS-LB with a 22G fork-tip core biopsy needle can be accurately used to stage non-alcoholic fatty liver disease (NAFLD) and may be superior to magnetic resonance elastography (MRE) in detecting early fibrosis is NASH. The median TSL was 2.4 cm, median CPT was 26 and 100% of samples achieved adequacy in staging fibrosis.

Comparison of diagnostic samples by needle: EUS-FNA vs EUS-FNB

Different authors have conducted comparative evaluations of EUS-LB with FNA and FNB in attempt to establish a pattern of superiority. In a large 2017 study, Schulman *et al*[79] directly compared the histologic samples of six different LB needles (19G Expect FNA needle, 19G SharkCore FNB needle, 22G SharkCore FNB needle, 19G Procore FNB needle and two 18-G PC needles) that were used on human cadavers. The mean number of CPTs (6.2) was significantly higher in specimens taken with the novel 19G SharkCore FNB needle. Similarly, both the 22G and 19G SharkCore FNB needle achieved the highest specimen adequacy and percent of core samples, suggesting

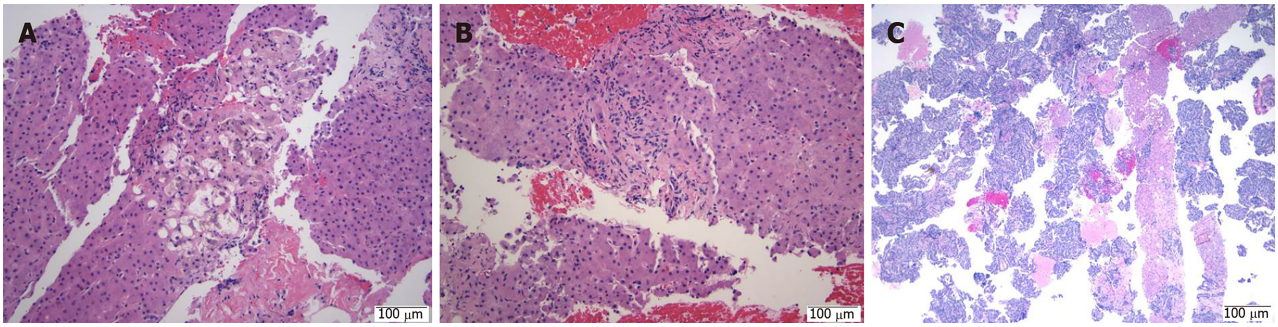

Figure 2 Histology of liver biopsy from the endoscopic ultrasound approach. A: Liver parenchyma with macrovesicular steatosis and focal ballooning degeneration (200× magnification, hematoxylin-eosin staining); B: Liver parenchyma with portal tract (center, 200× magnification, hematoxylin-eosin staining); C: Liver biopsy performed to target a mass lesion that was a clinically suspected metastasis (40× magnification, hematoxylin-eosin staining). The majority of the biopsy is composed of pleomorphic epithelioid cells in sheets and trabeculae that was suggestive of metastatic germ cell tumor.

superiority to the PC and 19G FNA needle in EUS-LB. Another recent study (n = 20) by Mok *et al*[80] evaluated tissue adequacy of a 22G FNB needle and a 19G FNA needle and found that the 19G FNA needle had greater tissue adequacy. However, a major limitation of this study is that the authors compared two different types of needles and two different gauges, making it difficult to conclude that the findings observed in this study were due differences in gauges and not the result of both variables compounded.

A meta-analysis by Khan *et al*[81] found similar diagnostic yield between EUS-FNA and EUS-FNB, but only when ROSE was used with FNA. Without ROSE, FNB produced better diagnostic adequacy in solid lesions and required fewer passes to reach a diagnosis. Similarly, another meta-analysis of studies comparing sample quality between the FNB ProCore needle and the standard FNA needle also showed comparable sampling and diagnostic results. However, the ProCore needle was able to obtain a diagnosis with fewer passes[82]. To further compare, a prospective trial (n = 40) of EUS-LBs demonstrated that 19G FNB needles produced specimens with longer specimen length, longer pieces of tissue core and more CPTs compared to 19G FNA needles[83].

Tissue acquisition techniques

Different techniques of tissue acquisition have been proposed to improve the diagnostic yield of EUS-LB. Many endoscopists use suction techniques or a slow-pull technique with FNA[7]. Some of the common EUS-LB suction techniques include dry heparin, dry suction technique (DRST) and wet suction technique (WEST). High negative pressure suction with an air-filled pre-vacuum syringe has been used in conventional EUS-FNA, but diminishes the sample quality by increasing the amount of blood in the specimen[84]. The WEST, on the other hand, was designed to address this specific issue and improve tissue yield. The WEST essentially uses pre-flushed saline instead of air. A prospective study found significantly greater cellularity and improved diagnostic yield in the WEST compared to DRST[85]. Similarly, use of a heparinized needle to prevent coagulation has been shown to improve tissue yield for EUS-LB. In a 2018 prospective study (n = 40) by Mok *et al*[53], three LB samples were taken from each patient, using the DRST, dry heparin and wet heparin techniques. Specimens taken with the wet heparin suction technique had less tissue fragmentation, produced more CPTs, and maintained increased aggregate specimen length and longer lengths of the longest piece compared to both dry methods[53]. Other techniques used include the fanning technique, which is used to obtain more tissue with fewer passes and the slow pull technique, which relies upon the negative pressure within the needle as the stylet is being slowly removed by the assistant during FNA "throws"[86].

While these techniques are useful for EUS-FNA, few studies have explored techniques that can be applied when using newer FNB needles. The modified 1-pass 1 actuation wet suction technique, however, may show promise. One recent retrospective study (n = 165) described the modified 1-pass 1 actuation wet suction technique with a 19G EUS-FNB (SharkCore) needle in patients evaluated for abnormal liver chemistries. The median TSL was 6 cm and the mean of CPTs was 7.5 cm, suggesting an effective technique[76]. Saab *et al*[87] also concluded that the 19G core biopsy needle with the use of the modified one-pass wet suction technique was more accurate in diagnosing and staging NAFLD compared to MRE.

EUS-LB in special populations

Gastric bypass: Patients with altered anatomy, such as a gastric bypass, may also undergo EUS-LB safely and effectively. Amongst the cohort of patients evaluated for abnormal liver enzymes or liver disease in a prospective study by Diehl *et al*[51], 2/110 participants presented with a surgical history of a Roux-en-Y gastric bypass. Due to their altered anatomy, the right lobe of the liver was inaccessible. Therefore, EUS-LB of only the left lobe was taken, albeit successfully, through the transgastric approach, with sufficient tissue to render a diagnosis, and no procedural complications[51].

Liver transplant patients: Patients with a history of liver transplantation comprise a unique group in which LB may be required. Indications for LB in this population include histologic evaluation (in pre-transplant liver donors), monitoring for evidence of graft injury, confirming a diagnosis in patients with acutely abnormal LFTs, assessing the degree of injury or fibrosis, and monitoring changes following therapeutic intervention[88]. A retrospective study, in which nearly a quarter of participants were liver transplant patients, found that EUS-LB was safe and effective in evaluating post liver transplant patients with abnormal liver chemistries. EUS-LB was performed successfully with a 19G core needle via modified wet suction technique, with no complications or adverse events noted in the transplant group[89]. Multiple larger studies are needed to clearly identify the role of EUS-LB in post-transplant patients as they pose unique challenges in terms of post-surgery status, anatomical variations and higher risk of post procedure infections.

Pediatric patients: Much of the existing literature regarding the efficacy of EUS-LB is limited to studies pertaining to the adult population, but very few studies have evaluated the use of EUS-LB in the pediatric population. Johal *et al*[90] reported the first known case series (n = 3) demonstrating the usefulness and safety of EUS-LB in three pediatric subjects who were evaluated for persistently elevated liver enzymes of unclear etiology. The biopsy was successfully performed with a 19G EUS-FNA needle and allowed for good histological return in all three cases yielding CPTs of 20, 31 and 16, and a tissue lengths of 30 mm, 53 mm and 62 mm. No procedure related adverse events or complications were noted in any of the children. Additional studies in this particular population are needed, but preliminary reports suggest that EUS-LB in pediatric patients is safe and effective[90].

CONCLUSION

LB is an essential tool in diagnosing, evaluating and treating various diseases of the liver. While the traditional PCLB and TJLB methods are established and have been used extensively, there are some disadvantages to their use. Thus, EUS-LB represents a more novel, effective and safe alternative to obtaining hepatic tissue with several advantages. EUS-LB allows for detection of smaller lesions and bi-lobar liver sampling, which in turn improves tissue yield and obtains more representative sampling, allowing for greater diagnostic potential. The use of real time imaging guidance with doppler also helps reduce inadvertent injury to pertinent anatomic structures and procedure related complications. While cost and availability of expertise are possible barriers to the widespread use of this technique, EUS-LB offers several benefits that should be given appropriate weight when choosing a method of LB. More evidence is needed in terms of multi-center trials with randomization before this technique can be adopted as a new standard.

REFERENCES

1 **Bravo AA**, Sheth SG, Chopra S. Liver biopsy. *N Engl J Med* 2001; **344**: 495-500 [PMID: 11172192 DOI: 10.1056/NEJM200102153440706]

2 **Rockey DC**, Caldwell SH, Goodman ZD, Nelson RC, Smith AD; American Association for the Study of Liver Diseases. Liver biopsy. *Hepatology* 2009; **49**: 1017-1044 [PMID: 19243014 DOI: 10.1002/hep.22742]

3 **Larrey D**, Meunier L, Ursic-Bedoya J. Liver Biopsy in Chronic Liver Diseases: Is There a Favorable Benefit: Risk Balance? *Ann Hepatol* 2017; **16**: 487-489 [PMID: 28612749 DOI: 10.5604/01.3001.0010.0272]

4 **Skelly MM**, James PD, Ryder SD. Findings on liver biopsy to investigate abnormal liver function tests in the absence of diagnostic serology. *J Hepatol* 2001; **35**: 195-199 [PMID: 11580141]

5 **Kalambokis G**, Manousou P, Vibhakorn S, Marelli L, Cholongitas E, Senzolo M, Patch D, Burroughs AK. Transjugular liver biopsy--indications, adequacy, quality of specimens, and complications--a systematic review. *J Hepatol* 2007; **47**: 284-294 [PMID: 17561303 DOI: 10.1016/j.jhep.2007.05.001]

6 **Dohan A**, Guerrache Y, Boudiaf M, Gavini JP, Kaci R, Soyer P. Transjugular liver biopsy: indications, technique and results. *Diagn Interv Imaging* 2014; **95**: 11-15 [PMID: 24007769 DOI:

10.1016/j.diii.2013.08.009]
7 **West J**, Card TR. Reduced mortality rates following elective percutaneous liver biopsies. *Gastroenterology* 2010; **139**: 1230-1237 [PMID: 20547160 DOI: 10.1053/j.gastro.2010.06.015]
8 **Myers RP**, Fong A, Shaheen AA. Utilization rates, complications and costs of percutaneous liver biopsy: a population-based study including 4275 biopsies. *Liver Int* 2008; **28**: 705-712 [PMID: 18433397 DOI: 10.1111/j.1478-3231.2008.01691.x]
9 **Seeff LB**, Everson GT, Morgan TR, Curto TM, Lee WM, Ghany MG, Shiffman ML, Fontana RJ, Di Bisceglie AM, Bonkovsky HL, Dienstag JL; HALT–C Trial Group. Complication rate of percutaneous liver biopsies among persons with advanced chronic liver disease in the HALT-C trial. *Clin Gastroenterol Hepatol* 2010; **8**: 877-883 [PMID: 20362695 DOI: 10.1016/j.cgh.2010.03.025]
10 **Regev A**, Berho M, Jeffers LJ, Milikowski C, Molina EG, Pyrsopoulos NT, Feng ZZ, Reddy KR, Schiff ER. Sampling error and intraobserver variation in liver biopsy in patients with chronic HCV infection. *Am J Gastroenterol* 2002; **97**: 2614-2618 [PMID: 12385448 DOI: 10.1111/j.1572-0241.2002.06038.x]
11 **Shah AR**, Al-Hanayneh M, Chowdhry M, Bilal M, Singh S. Endoscopic ultrasound guided liver biopsy for parenchymal liver disease. *World J Hepatol* 2019; **11**: 335-343 [PMID: 31114638 DOI: 10.4254/wjh.v11.i4.335]
12 **Saraireh HA**, Bilal M, Singh S. Role of endoscopic ultrasound in liver disease: Where do we stand in 2017? *World J Hepatol* 2017; **9**: 1013-1021 [PMID: 28932347 DOI: 10.4254/wjh.v9.i24.1013]
13 **Diehl DL**. Endoscopic Ultrasound-guided Liver Biopsy. *Gastrointest Endosc Clin N Am* 2019; **29**: 173-186 [PMID: 30846147 DOI: 10.1016/j.giec.2018.11.002]
14 **Stölzel U**, Tannapfel A. [Indications for liver biopsy in liver tumors]. *Zentralbl Chir* 2000; **125**: 606-609 [PMID: 10960970]
15 **Suzuki A**, Brunt EM, Kleiner DE, Miquel R, Smyrk TC, Andrade RJ, Lucena MI, Castiella A, Lindor K, Björnsson E. The use of liver biopsy evaluation in discrimination of idiopathic autoimmune hepatitis versus drug-induced liver injury. *Hepatology* 2011; **54**: 931-939 [PMID: 21674554 DOI: 10.1002/hep.24481]
16 **Tannapfel A**, Dienes HP, Lohse AW. The indications for liver biopsy. *Dtsch Arztebl Int* 2012; **109**: 477-483 [PMID: 22833761 DOI: 10.3238/arztebl.2012.0477]
17 **Pietrangelo A**. Hereditary hemochromatosis: pathogenesis, diagnosis, and treatment. *Gastroenterology* 2010; **139**: 393-408, 408.e1-408.e2 [PMID: 20542038 DOI: 10.1053/j.gastro.2010.06.013]
18 **Pelz L**. [Diagnostic liver puncture in the work of Paul Ehrlich]. *Med Monatsschr* 1965; **19**: 357-359 [PMID: 5326954]
19 **Parekh PJ**, Majithia R, Diehl DL, Baron TH. Endoscopic ultrasound-guided liver biopsy. *Endosc Ultrasound* 2015; **4**: 85-91 [PMID: 26020041 DOI: 10.4103/2303-9027.156711]
20 **Gilmore IT**, Burroughs A, Murray-Lyon IM, Williams R, Jenkins D, Hopkins A. Indications, methods, and outcomes of percutaneous liver biopsy in England and Wales: an audit by the British Society of Gastroenterology and the Royal College of Physicians of London. *Gut* 1995; **36**: 437-441 [PMID: 7698705 DOI: 10.1136/gut.36.3.437]
21 **Abdi W**, Millan JC, Mezey E. Sampling variability on percutaneous liver biopsy. *Arch Intern Med* 1979; **139**: 667-669 [PMID: 443970]
22 **McGill DB**, Rakela J, Zinsmeister AR, Ott BJ. A 21-year experience with major hemorrhage after percutaneous liver biopsy. *Gastroenterology* 1990; **99**: 1396-1400 [PMID: 2101588]
23 **Sparchez Z**. Complications after percutaneous liver biopsy in diffuse hepatopathies. *Rom J Gastroenterol* 2005; **14**: 379-384 [PMID: 16400355]
24 **Caldwell S**, Northup PG. Bleeding complication with liver biopsy: is it predictable? *Clin Gastroenterol Hepatol* 2010; **8**: 826-829 [PMID: 20601136 DOI: 10.1016/j.cgh.2010.06.010]
25 **Eisenberg E**, Konopniki M, Veitsman E, Kramskay R, Gaitini D, Baruch Y. Prevalence and characteristics of pain induced by percutaneous liver biopsy. *Anesth Analg* 2003; **96**: 1392-1396, table of contents [PMID: 12707140]
26 **Veneri RJ**, Gordon SC, Fink-Bennett D. Scintigraphic and culdoscopic diagnosis of bile peritonitis complicating liver biopsy. *J Clin Gastroenterol* 1989; **11**: 571-573 [PMID: 2794437]
27 **Janes CH**, Lindor KD. Outcome of patients hospitalized for complications after outpatient liver biopsy. *Ann Intern Med* 1993; **118**: 96-98 [PMID: 8416324 DOI: 10.7326/0003-4819-118-2-199301150-00003]
28 **Gambarin-Gelwan M**. Percutaneous Liver Biopsy. *Gastroenterol Hepatol (N Y)* 2006; **2**: 689-690 [PMID: 28316539]
29 **Chahal PS**, Ready J. Hemothorax after percutaneous liver biopsy: an unusual complication. *Am J Gastroenterol* 2002; **97**: 1068-1069 [PMID: 12003398 DOI: 10.1111/j.1572-0241.2002.05638.x]
30 **Sheth D**, Pillai A, Ferral H, Madassery S. Transient bacteremia after a percutaneous liver biopsy. *J Vasc Interv Radiol* 2009; **20**: 1429-1430 [PMID: 19875059 DOI: 10.1016/j.jvir.2009.08.004]
31 **Piccinino F**, Sagnelli E, Pasquale G, Giusti G. Complications following percutaneous liver biopsy. A multicentre retrospective study on 68,276 biopsies. *J Hepatol* 1986; **2**: 165-173 [PMID: 3958472]
32 **Procopet B**, Bureau C, Métivier S, Selves J, Robic MA, Christol C, Grigorescu M, Vinel JP, Péron JM. Tolerance of liver biopsy in a tertiary care center: comparison of the percutaneous and the transvenous route in 143 prospectively followed patients. *Eur J Gastroenterol Hepatol* 2012; **24**: 1209-1213 [PMID: 22668874 DOI: 10.1097/MEG.0b013e328355e2ba]
33 **Cholongitas E**, Senzolo M, Standish R, Marelli L, Quaglia A, Patch D, Dhillon AP, Burroughs AK. A systematic review of the quality of liver biopsy specimens. *Am J Clin Pathol* 2006; **125**: 710-721 [PMID: 16707372 DOI: 10.1309/W3XC-NT4H-KFBN-2G0B]
34 **Dotter CT**. Catheter biopsy. Experimental technic for transvenous liver biopsy. *Radiology* 1964; **82**: 312-314 [PMID: 14115317 DOI: 10.1148/82.2.312]
35 **Gamble P**, Colapinto RF, Stronell RD, Colman JC, Blendis L. Transjugular liver biopsy: a review of 461 biopsies. *Radiology* 1985; **157**: 589-593 [PMID: 4059543 DOI: 10.1148/radiology.157.3.4059543]
36 **Behrens G**, Ferral H. Transjugular liver biopsy. *Semin Intervent Radiol* 2012; **29**: 111-117 [PMID: 23729981 DOI: 10.1055/s-0032-1312572]
37 **Miraglia R**, Luca A, Gruttadauria S, Minervini MI, Vizzini G, Arcadipane A, Gridelli B. Contribution of transjugular liver biopsy in patients with the clinical presentation of acute liver failure. *Cardiovasc Intervent Radiol* 2006; **29**: 1008-1010 [PMID: 16967214 DOI: 10.1007/s00270-006-0052-5]
38 **Donaldson BW**, Gopinath R, Wanless IR, Phillips MJ, Cameron R, Roberts EA, Greig PD, Levy G, Blendis LM. The role of transjugular liver biopsy in fulminant liver failure: relation to other prognostic indicators. *Hepatology* 1993; **18**: 1370-1376 [PMID: 8244261]
39 **Mammen T**, Keshava SN, Eapen CE, Raghuram L, Moses V, Gopi K, Babu NS, Ramachandran J, Kurien

G. Transjugular liver biopsy: a retrospective analysis of 601 cases. *J Vasc Interv Radiol* 2008; **19**: 351-358 [PMID: 18295693 DOI: 10.1016/j.jvir.2007.09.002]
40 **Saab S**, Cho D, Quon DV, Ibrahim AB, Dong P, Marder V, Logan L. Same day outpatient transjugular liver biopsies in haemophilia. *Haemophilia* 2004; **10**: 727-731 [PMID: 15569168 DOI: 10.1111/j.1365-2516.2004.01043.x]
41 **Ble M**, Procopet B, Miquel R, Hernandez-Gea V, García-Pagán JC. Transjugular liver biopsy. *Clin Liver Dis* 2014; **18**: 767-778 [PMID: 25438282 DOI: 10.1016/j.cld.2014.07.001]
42 **Campbell MS**, Reddy KR. Review article: the evolving role of liver biopsy. *Aliment Pharmacol Ther* 2004; **20**: 249-259 [PMID: 15274661 DOI: 10.1111/j.1365-2036.2004.02071.x]
43 **Denzer U**, Arnoldy A, Kanzler S, Galle PR, Dienes HP, Lohse AW. Prospective randomized comparison of minilaparoscopy and percutaneous liver biopsy: diagnosis of cirrhosis and complications. *J Clin Gastroenterol* 2007; **41**: 103-110 [PMID: 17198072 DOI: 10.1097/01.mcg.0000225612.86846.82]
44 **Vargas C**, Jeffers LJ, Bernstein D, Reddy KR, Munnangi S, Behar S, Scott C, Parker T, Schiff ER. Diagnostic laparoscopy: a 5-year experience in a hepatology training program. *Am J Gastroenterol* 1995; **90**: 1258-1262 [PMID: 7639226]
45 **Poniachik J**, Bernstein DE, Reddy KR, Jeffers LJ, Coelho-Little ME, Civantos F, Schiff ER. The role of laparoscopy in the diagnosis of cirrhosis. *Gastrointest Endosc* 1996; **43**: 568-571 [PMID: 8781934 DOI: 10.1016/s0016-5107(96)70192-x]
46 **Lohse AW**. Rolls Royce for everybody? Diagnosing liver disease by mini-laparoscopy. *J Hepatol* 2011; **54**: 584-585 [PMID: 21159402 DOI: 10.1016/j.jhep.2010.09.033]
47 **Friedberg SR**, Lachter J. Endoscopic ultrasound: Current roles and future directions. *World J Gastrointest Endosc* 2017; **9**: 499-505 [PMID: 29085560 DOI: 10.4253/wjge.v9.i10.499]
48 **DiMagno EP**, Buxton JL, Regan PT, Hattery RR, Wilson DA, Suarez JR, Green PS. Ultrasonic endoscope. *Lancet* 1980; **1**: 629-631 [PMID: 6102631 DOI: 10.1016/s0140-6736(80)91122-8]
49 **Gress FG**. The Early History of Interventional Endoscopic Ultrasound. *Gastrointest Endosc Clin N Am* 2017; **27**: 547-550 [PMID: 28918797 DOI: 10.1016/j.giec.2017.06.015]
50 **Mohan BP**, Shakhatreh M, Garg R, Ponnada S, Adler DG. Efficacy and safety of EUS-guided liver biopsy: a systematic review and meta-analysis. *Gastrointest Endosc* 2019; **89**: 238-246.e3 [PMID: 30389469 DOI: 10.1016/j.gie.2018.10.018]
51 **Diehl DL**, Johal AS, Khara HS, Stavropoulos SN, Al-Haddad M, Ramesh J, Varadarajulu S, Aslanian H, Gordon SR, Shieh FK, Pineda-Bonilla JJ, Dunkelberger T, Gondim DD, Chen EZ. Endoscopic ultrasound-guided liver biopsy: a multicenter experience. *Endosc Int Open* 2015; **3**: E210-E215 [PMID: 26171433 DOI: 10.1055/s-0034-1391412]
52 **Adler DG**, Muthusamy VR, Ehrlich DS, Parasher G, Thosani NC, Chen A, Buscaglia JM, Appannagari A, Quintero E, Aslanian H, Taylor LJ, Siddiqui A. A multicenter evaluation of a new EUS core biopsy needle: Experience in 200 patients. *Endosc Ultrasound* 2019; **8**: 99-104 [PMID: 29623911 DOI: 10.4103/eus.eus_53_17]
53 **Mok SRS**, Diehl DL, Johal AS, Khara HS, Confer BD, Mudireddy PR, Kirchner HL, Chen ZE. A prospective pilot comparison of wet and dry heparinized suction for EUS-guided liver biopsy (with videos). *Gastrointest Endosc* 2018; **88**: 919-925 [PMID: 30120956 DOI: 10.1016/j.gie.2018.07.036]
54 **Gleeson FC**, Levy MJ. EUS Trucut biopsy liver parenchyma acquisition and yield are comparable to that of a transjugular liver biopsy. *Gastrointest Endosc* 2009; **70**: 1046; author reply 1046-1046; author reply 1047 [PMID: 19879410 DOI: 10.1016/j.gie.2009.03.030]
55 **Stavropoulos SN**, Im GY, Jlayer Z, Harris MD, Pitea TC, Turi GK, Malet PF, Friedel DM, Grendell JH. High yield of same-session EUS-guided liver biopsy by 19-gauge FNA needle in patients undergoing EUS to exclude biliary obstruction. *Gastrointest Endosc* 2012; **75**: 310-318 [PMID: 22248599 DOI: 10.1016/j.gie.2011.09.043]
56 **ASGE Technology committee**, Tierney WM, Adler DG, Chand B, Conway JD, Croffie JM, DiSario JA, Mishkin DS, Shah RJ, Somogyi L, Wong Kee Song LM, Petersen BT. Echoendoscopes. *Gastrointest Endosc* 2007; **66**: 435-442 [PMID: 17640635 DOI: 10.1016/j.gie.2007.05.028]
57 **Oh D**, Seo DW, Hong SM, Song TJ, Park DH, Lee SS, Lee SK, Kim MH. Endoscopic ultrasound-guided fine-needle aspiration can target right liver mass. *Endosc Ultrasound* 2017; **6**: 109-115 [PMID: 28440236 DOI: 10.4103/2303-9027.204813]
58 **Nguyen P**, Feng JC, Chang KJ. Endoscopic ultrasound (EUS) and EUS-guided fine-needle aspiration (FNA) of liver lesions. *Gastrointest Endosc* 1999; **50**: 357-361 [PMID: 10462656 DOI: 10.1053/ge.1999.v50.97208]
59 **Awad SS**, Fagan S, Abudayyeh S, Karim N, Berger DH, Ayub K. Preoperative evaluation of hepatic lesions for the staging of hepatocellular and metastatic liver carcinoma using endoscopic ultrasonography. *Am J Surg* 2002; **184**: 601-604; discussion 604-605 [PMID: 12488184 DOI: 10.1016/s0002-9610(02)01092-9]
60 **Singh P**, Mukhopadhyay P, Bhatt B, Patel T, Kiss A, Gupta R, Bhat S, Erickson RA. Endoscopic ultrasound versus CT scan for detection of the metastases to the liver: results of a prospective comparative study. *J Clin Gastroenterol* 2009; **43**: 367-373 [PMID: 18981929 DOI: 10.1097/MCG.0b013e318167b8cc]
61 **Vilmann P**, Krasnik M, Larsen SS, Jacobsen GK, Clementsen P. Transesophageal endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) and endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) biopsy: a combined approach in the evaluation of mediastinal lesions. *Endoscopy* 2005; **37**: 833-839 [PMID: 16116534 DOI: 10.1055/s-2005-870276]
62 **Takyar V**, Etzion O, Heller T, Kleiner DE, Rotman Y, Ghany MG, Fryzek N, Williams VH, Rivera E, Auh S, Liang TJ, Hoofnagle JH, Koh C. Complications of percutaneous liver biopsy with Klatskin needles: a 36-year single-centre experience. *Aliment Pharmacol Ther* 2017; **45**: 744-753 [PMID: 28074540 DOI: 10.1111/apt.13939]
63 **Sue M**, Caldwell SH, Dickson RC, Macalindong C, Rourk RM, Charles C, Doobay R, Cambridge SL, Barritt AS, McCallum RW. Variation between centers in technique and guidelines for liver biopsy. *Liver* 1996; **16**: 267-270 [PMID: 8877999]
64 **Cazacu IM**, Luzuriaga Chavez AA, Saftoiu A, Vilmann P, Bhutani MS. A quarter century of EUS-FNA: Progress, milestones, and future directions. *Endosc Ultrasound* 2018; **7**: 141-160 [PMID: 29941723 DOI: 10.4103/eus.eus_19_18]
65 **Colloredo G**, Guido M, Sonzogni A, Leandro G. Impact of liver biopsy size on histological evaluation of chronic viral hepatitis: the smaller the sample, the milder the disease. *J Hepatol* 2003; **39**: 239-244 [PMID: 12873821]

66 **Pineda JJ**, Diehl DL, Miao CL, Johal AS, Khara HS, Bhanushali A, Chen EZ. EUS-guided liver biopsy provides diagnostic samples comparable with those via the percutaneous or transjugular route. *Gastrointest Endosc* 2016; **83**: 360-365 [PMID: 26301407 DOI: 10.1016/j.gie.2015.08.025]

67 **Lee YN**, Moon JH, Kim HK, Choi HJ, Choi MH, Kim DC, Lee TH, Lee TH, Cha SW, Kim SG, Kim YS. Usefulness of endoscopic ultrasound-guided sampling using core biopsy needle as a percutaneous biopsy rescue for diagnosis of solid liver mass: Combined histological-cytological analysis. *J Gastroenterol Hepatol* 2015; **30**: 1161-1166 [PMID: 25684303 DOI: 10.1111/jgh.12922]

68 **Shuja A**, Alkhasawneh A, Fialho A, Fialho A, Shukri A, Harris C, Smotherman C, Malespin M, de Melo SW. Comparison of EUS-guided versus percutaneous and transjugular approaches for the performance of liver biopsies. *Dig Liver Dis* 2019; **51**: 826-830 [PMID: 30755347 DOI: 10.1016/j.dld.2019.01.006]

69 **Rombaoa C**, Chen, Ann M. The Safety and Feasibilty of Endoscopic Ultrasound-Guided Parenchymal Liver Biopsy At A Large Community Hospital. *Gastrointest Endosc* 2018; **87**: AB458 [DOI: 10.1016/j.gie.2018.04.2001]

70 **Wiersema MJ**, Levy MJ, Harewood GC, Vazquez-Sequeiros E, Jondal ML, Wiersema LM. Initial experience with EUS-guided trucut needle biopsies of perigastric organs. *Gastrointest Endosc* 2002; **56**: 275-278 [PMID: 12145612 DOI: 10.1016/s0016-5107(02)70193-4]

71 **Dewitt J**, McGreevy K, Cummings O, Sherman S, Leblanc JK, McHenry L, Al-Haddad M, Chalasani N. Initial experience with EUS-guided Tru-cut biopsy of benign liver disease. *Gastrointest Endosc* 2009; **69**: 535-542 [PMID: 19231495 DOI: 10.1016/j.gie.2008.09.056]

72 **Sey MS**, Al-Haddad M, Imperiale TF, McGreevy K, Lin J, DeWitt JM. EUS-guided liver biopsy for parenchymal disease: a comparison of diagnostic yield between two core biopsy needles. *Gastrointest Endosc* 2016; **83**: 347-352 [PMID: 26278654 DOI: 10.1016/j.gie.2015.08.012]

73 **Gor N**, Salem SB, Jakate S, Patel R, Shah N, Patil A. Histological adequacy of EUS-guided liver biopsy when using a 19-gauge non-Tru-Cut FNA needle. *Gastrointest Endosc* 2014; **79**: 170-172 [PMID: 23916397 DOI: 10.1016/j.gie.2013.06.031]

74 **Ichim VA**, Chira RI, Mircea PA. Diagnostic yield of endoscopic ultrasound-guided biopsy of focal liver lesions. *Med Pharm Rep* 2019; **92**: 15-20 [PMID: 30957081 DOI: 10.15386/cjmed-1066]

75 **Shah ND**, Sasatomi E, Baron TH. Endoscopic Ultrasound-guided Parenchymal Liver Biopsy: Single Center Experience of a New Dedicated Core Needle. *Clin Gastroenterol Hepatol* 2017; **15**: 784-786 [PMID: 28126424 DOI: 10.1016/j.cgh.2017.01.011]

76 **Nieto J**, Khaleel H, Challita Y, Jimenez M, Baron TH, Walters L, Hathaway K, Patel K, Lankarani A, Herman M, Holloman D, Saab S. EUS-guided fine-needle core liver biopsy sampling using a novel 19-gauge needle with modified 1-pass, 1 actuation wet suction technique. *Gastrointest Endosc* 2018; **87**: 469-475 [PMID: 28551024 DOI: 10.1016/j.gie.2017.05.013]

77 **Hasan MK**, Kadkhodayan K, Idrisov E, Ali S, Rafiq E, Ben-Ami Shor D, Abdel-Jalil A, Navaneethan U, Bang J, Varadarajulu S, Hawes R, Pernicone P. Endoscopic ultrasound-guided liver biopsy using a 22-G fine needle biopsy needle: a prospective study. *Endoscopy* 2019; **51**: 818-824 [PMID: 31365947 DOI: 10.1055/a-0967-3640]

78 **Bazerbachi F**, Vargas EJ, Matar R, Storm AC, Mounajjed TM, Topazian MD, Levy MJ, Chandrasekhara V, Abu Dayyeh BK. EUS-guided core liver biopsy sampling using a 22-gauge fork-tip needle: a prospective blinded trial for histologic and lipidomic evaluation in nonalcoholic fatty liver disease. *Gastrointest Endosc* 2019; **90**: 926-932 [PMID: 31437454 DOI: 10.1016/j.gie.2019.08.006]

79 **Schulman AR**, Thompson CC, Odze R, Chan WW, Ryou M. Optimizing EUS-guided liver biopsy sampling: comprehensive assessment of needle types and tissue acquisition techniques. *Gastrointest Endosc* 2017; **85**: 419-426 [PMID: 27530070 DOI: 10.1016/j.gie.2016.07.065]

80 **Mok SRS**, Diehl DL, Johal AS, Khara HS, Confer BD, Mudireddy PR, Kovach AH, Diehl MM, Kirchner HL, Chen ZE. Endoscopic ultrasound-guided biopsy in chronic liver disease: a randomized comparison of 19-G FNA and 22-G FNB needles. *Endosc Int Open* 2019; **7**: E62-E71 [PMID: 30648141 DOI: 10.1055/a-0655-7462]

81 **Khan MA**, Grimm IS, Ali B, Nollan R, Tombazzi C, Ismail MK, Baron TH. A meta-analysis of endoscopic ultrasound-fine-needle aspiration compared to endoscopic ultrasound-fine-needle biopsy: diagnostic yield and the value of onsite cytopathological assessment. *Endosc Int Open* 2017; **5**: E363-E375 [PMID: 28497108 DOI: 10.1055/s-0043-101693]

82 **Bang JY**, Hawes R, Varadarajulu S. A meta-analysis comparing ProCore and standard fine-needle aspiration needles for endoscopic ultrasound-guided tissue acquisition. *Endoscopy* 2016; **48**: 339-349 [PMID: 26561917 DOI: 10.1055/s-0034-1393354]

83 **Ching-Companioni RA**, Diehl DL, Johal AS, Confer BD, Khara HS. 19G aspiration needle versus 19G core biopsy needle for endoscopic ultrasound-guided liver biopsy: a prospective randomized trial. *Endoscopy* 2019; **51**: 1059-1065 [PMID: 31342474 DOI: 10.1055/a-0956-6922]

84 **Wallace MB**, Kennedy T, Durkalski V, Eloubeidi MA, Etamad R, Matsuda K, Lewin D, Van Velse A, Hennesey W, Hawes RH, Hoffman BJ. Randomized controlled trial of EUS-guided fine needle aspiration techniques for the detection of malignant lymphadenopathy. *Gastrointest Endosc* 2001; **54**: 441-447 [PMID: 11577304 DOI: 10.1067/mge.2001.117764]

85 **Attam R**, Arain MA, Bloechl SJ, Trikudanathan G, Munigala S, Bakman Y, Singh M, Wallace T, Henderson JB, Catalano MF, Guda NM. "Wet suction technique (WEST)": a novel way to enhance the quality of EUS-FNA aspirate. Results of a prospective, single-blind, randomized, controlled trial using a 22-gauge needle for EUS-FNA of solid lesions. *Gastrointest Endosc* 2015; **81**: 1401-1407 [PMID: 25733127 DOI: 10.1016/j.gie.2014.11.023]

86 **Kin T**, Katanuma A, Yane K, Takahashi K, Osanai M, Takaki R, Matsumoto K, Gon K, Matsumori T, Tomonari A, Maguchi H, Shinohara T, Nojima M. Diagnostic ability of EUS-FNA for pancreatic solid lesions with conventional 22-gauge needle using the slow pull technique: a prospective study. *Scand J Gastroenterol* 2015; **50**: 900-907 [PMID: 25732902 DOI: 10.3109/00365521.2014.983155]

87 **Saab S**, Phan J, Jimenez MA, Grotts JF, Walters L, Hathaway KA, Patel KR, Lankarani A, Herman M, Holloman DA, Nieto JM. Endoscopic Ultrasound Liver Biopsies Accurately Predict the Presence of Fibrosis in Patients With Fatty liver. *Clin Gastroenterol Hepatol* 2017; **15**: 1477-1478 [PMID: 28419859 DOI: 10.1016/j.cgh.2017.04.017]

88 **Adeyi O**, Fischer SE, Guindi M. Liver allograft pathology: approach to interpretation of needle biopsies with clinicopathological correlation. *J Clin Pathol* 2010; **63**: 47-74 [PMID: 19847014 DOI: 10.1136/jcp.2009.068254]

89 **Alsaiari AA**, Therapondos G, Romero R, John Evans J, Shah JN, Cohen A, Galliano G, El Chafic AH. Endoscopic Ultrasound-Guided Liver Biopsy: A Tertiary Center Experience. *Gastrointest Endosc* 2018;

87: AB339-AB40 [DOI: 10.1016/j.gie.2018.04.1726]
90 **Johal AS**, Khara HS, Maksimak MG, Diehl DL. Endoscopic ultrasound-guided liver biopsy in pediatric patients. *Endosc Ultrasound* 2014; **3**: 191-194 [PMID: 25184126 DOI: 10.4103/2303-9027.138794]

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ORIGINAL ARTICLE

Prospective Study

Impact of a simulation-based induction programme in gastroscopy on trainee outcomes and learning curves

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Abstract

BACKGROUND

Pre-clinical simulation-based training (SBT) in endoscopy has been shown to augment trainee performance in the short-term, but longer-term data are lacking.

AIM

To assess the impact of a two-day gastroscopy induction course combining theory and SBT (Structured PRogramme of INduction and Training – SPRINT) on trainee outcomes over a 16-mo period.

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METHODS
This prospective case-control study compared outcomes between novice SPRINT attendees and controls matched from a United Kingdom training database. Study outcomes comprised: (1) Unassisted D2 intubation rates; (2) Procedural discomfort scores; (3) Sedation practice; (4) Time to 200 procedures; and (5) Time to certification.

RESULTS
Total 15 cases and 24 controls were included, with mean procedure counts of 10 and 3 (P = 0.739) pre-SPRINT. Post-SPRINT, no significant differences between the groups were detected in long-term D2 intubation rates (P = 0.332) or discomfort scores (P = 0.090). However, the cases had a significantly higher rate of unsedated procedures than controls post-SPRINT (58% *vs* 44%, P = 0.018), which was maintained over the subsequent 200 procedures. Cases tended to perform procedures at a greater frequency than controls in the post-SPRINT period (median: 16.2 *vs* 13.8 per mo, P = 0.051), resulting in a significantly greater proportion of cases achieving gastroscopy certification by the end of follow up (75% *vs* 36%, P = 0.017).

CONCLUSION
In this pilot study, attendees of the SPRINT cohort tended to perform more procedures and achieved gastroscopy certification earlier than controls. These data support the role for wider evaluation of pre-clinical induction involving SBT.

Key words: Gastroscopy; Esophagogastroduodenoscopy; Endoscopy training; Induction; Competency development; Simulation

Core tip: Simulation-based training has been shown to improve short-term trainee outcomes, but longer-term data on trainee and patient-based outcomes are lacking. A 2-d induction programme covering fundamental theory and hands-on training can improve trainee confidence and shorten the time to achieve gastroscopy certification.

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INTRODUCTION

High quality training is a prelude to high quality endoscopy[1]. Within the United Kingdom (UK), quality assurance of endoscopy training is overseen by the Joint Advisory Group on Gastrointestinal Endoscopy (JAG)[2]. For most gastroenterologists, training in endoscopy begins with gastroscopy. The process of gastroscopy training requires considerable time and effort; on average, 187 procedures are required to achieve consistent gastroscopy completion rates (95%+ intubation to the second part of the duodenum – D2)[3] and 282 procedures (1.9 years) to attain JAG certification[4], which is a national requirement for independent practice. With the imminent "Shape of Training" reforms to UK gastroenterology training[5], which proposes to shorten the length of specialist training, endoscopy trainers need to re-evaluate training methods and tools, to deliver evidence-based training pathways which accelerate the development of competency in endoscopic procedures.

Simulation-based training (SBT) provides one solution to this challenge. Modern-day computerised virtual reality (VR) simulators are capable of delivering immersive training without risk of patient harm. The plethora of high-quality evidence attests to the short-term benefits of SBT in augmenting the acquisition of fundamental technical skills such as scope handling and tip control[6-8], which could shorten the learning curve. Additionally, data from colonoscopy training confirm that trainee endoscopists

incur more procedural discomfort during earlier stages of training[9]. Despite this, pre-clinical SBT is not readily available within the UK JAG training pathway, where hands-on training typically begins with patient-based gastroscopy at the discretion of supervising trainers. Hence, there is a need for a standardised induction programme which can ensure that beginners are sufficiently armed with the basic skills and knowledge before approaching patient-based training, in line with other international training pathways[10]. Data on the longer-term benefits of SBT on trainee and patient outcomes are lacking.

The Structured PRogramme of INduction and Training (SPRINT) is an induction programme consisting of a structured sequence of theory and hands-on training elements designed to optimise and accelerate the early phase of training in gastroscopy (Table 1). The didactic theory-based seminars are intended to complement SBT and cover fundamental aspects such as endoscope design/handling and basic lesion recognition. The EndoSim (Surgical Science, Gothenburg, Sweden) is a novel endoscopic VR simulator (Figure 1) which incorporates a customisable SBT curriculum and generates task-specific metrics, but has not been validated. In September 2017, a two-day gastroscopy Induction programme combining these foundation knowledge sessions with SBT was provided to medical and surgical trainees from three training deaneries. The primary aim of this training intervention was to assess whether this type of enhanced induction can accelerate competency development in novice trainees. The secondary aim was to evaluate whether EndoSim metrics could distinguish between trainees and experts in order to assess discriminative validity of the simulator.

MATERIALS AND METHODS

Study design

In this prospective multicentre study, trainees commencing gastroscopy training (ST3) from three UK training deaneries (regions) were enrolled to the augmented SBT induction programme. All trainees completed a structured curriculum of hands-on simulator training lasting a minimum of 3 h with feedback from JAG certified faculty trainers. This study had three components. First, trainee performance on the EndoSim VR simulator was compared to that of the expert faculty (all > 1000 procedures) to explore discriminative validity of the metrics used. To minimise bias, each participant's first valid attempt, without prior faculty training or feedback, was included. Training was only offered once all trainees had completed the assessment round. The second component was an assessment of the change in self-reported confidence scores following the course, based on questionnaires completed immediately pre- and post-course. The third component of the study assessed the impact of the course on long-term trainee outcomes using a case-control method. In the UK, all trainees are required to log training procedures onto the JAG Endoscopy Training System (JETS) e-portfolio[11]. Participation is mandated to enable certification for independent practice. For this analysis, a cohort of control trainees was selected from non-attenders who had submitted formative assessment data on JETS in the post-course period between September and December 2017. Only trainees with < 50 procedures, and whose first JETS-recorded procedure was less than a year prior to the date of SPRINT were included in the analyses of long-term outcomes, to ensure the levels of experience were similar in cases and controls. In addition, trainees with no gastroscopy procedures logged on JETS post-SPRINT were excluded, since these had not begun hands-on training in the post-course period. Trainee and patient outcomes for each post-course training procedure were extracted from the JETS e-portfolio, with prospective follow-up of outcomes post-SPRINT performed from September 2017 until February 2019 (maximum period of 16 mo).

Study approval

Study approval was granted by JAG Quality Assurance of Training working group. All participants provided written, informed consent for inclusion within the study. Neither the researchers nor Surgical Science had access to the study outcome data over the course of the study. There was no financial incentive to conduct this study.

Study outcomes

Discriminative validity of EndoSim: EndoSim scenarios and computer-generated metrics relevant to the assessment of technical skills in gastroscopy were selected as study outcomes for the first component of the study. Pre-set modules relevant to gastroscopy were selected, which generated skillset-dependent EndoSim metrics. Comparisons were then made between trainees and experts, followed by subgroup

Table 1 The Structured PRogramme of INduction and Training gastroscopy induction programme

Time	Programme	
8.3	**Coffee and registration**	
9	Welcome and introduction to aims and objectives	
9.3	Simulator session 1	Basic handling and scope design
10.2	Basic handling and scope design	Simulator session 1
11.1	**Coffee**	
11.3	Simulator session 2	JAG Certification, appraisal and training lists
12.2	JAG Certification, appraisal and training lists	Simulator session 2
13.1	**Lunch**	
13.4	Simulator session 3	Enhancing the endoscopic image
14.1	Enhancing the endoscopic image	Simulator session 3
15	**Coffee**	
15.2	Simulator session 4	Lesion recognition and assessment skills 1
16.1	Lesion recognition and assessment skills 1	Simulator session 4
17	Round up	
8.3	**Coffee and registration**	
9	Welcome and introduction to day 2	
9.1	Simulator session 5	Getting the best out of the JETS e-portfolio
10	Getting the best out of the JETS e-portfolio	Simulator session 5
10.5	**Coffee**	
11.1	Simulator session 6	Lesion recognition and assessment skills 2
12	Lesion recognition and assessment skills 2	Simulator session 2
12.5	**Lunch**	
13.2	Simulator session 7	Decision-making and report writing
13.5	Decision-making and report writing	Simulator session 7
14.4	**Coffee**	
15	Simulator session 8	DOPS assessment and improving your skills
15.5	DOPS assessment and improving your skills	Simulator session 8
16.4	Summary and review of course objectives	

DOPS: Direct observation of procedural skills.

analyses within the trainees, comparing novices (< 25 procedures) to those with intermediate experience (25 + procedures).

Impact on self-assessed competence scores: Questionnaires were administered to all trainees both pre- and post-course, which measured self-assessed competency scores in 12 upper GI handling skills domains. These domains were mapped to the formative JAG formative assessment forms which are integrated into UK endoscopy training[12]. Domain scores were given as a rating from 0-10 on a Likert scale (0 = not at all competent, 10 = very competent).

Long-term trainee outcomes: For the analysis of long-term trainee outcomes, the trainee outcomes included the unassisted rate of D2 intubation, *i.e.*, procedures without physical assistance, the volume of training procedures performed post-course, and the time taken to achieve JAG gastroscopy certification. JAG certification involves the composite outcome of attaining a minimum lifetime patient-based gastroscopy count (200+) and satisfactory completion of formative and summative direct observation of procedural skills assessments to objectively demonstrate competence[4,12,13]. Patient outcomes were also explored; these included comparisons in rates of moderate-to-severe discomfort and rates of unsedated procedures.

Statistical analyses

For the first two components of the study, variables were reported as medians and interquartile ranges (IQRs), and compared between groups using Mann-Whitney tests, with Wilcoxon's tests used for paired comparisons. For the third component, trends in study outcomes (*i.e.*, D2 intubation, sedation and discomfort rates) were

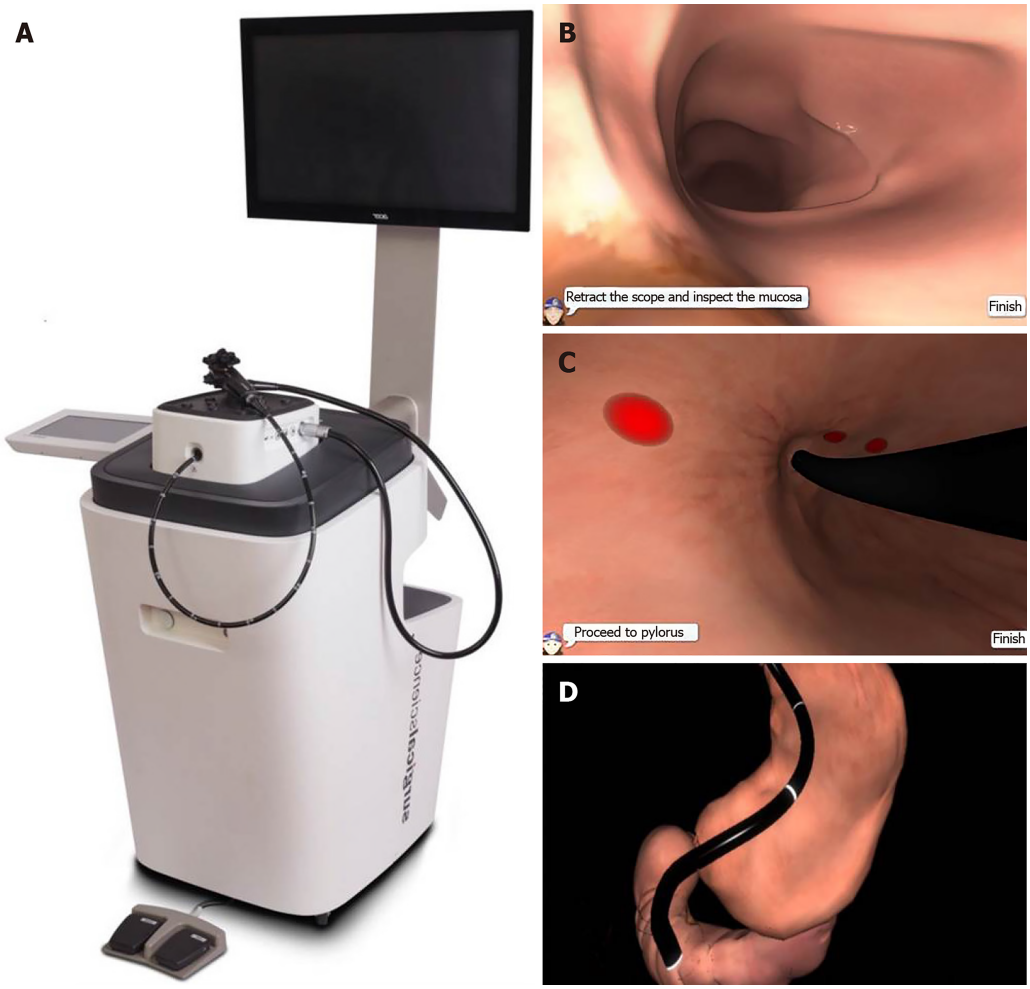

Figure 1 The surgical science EndoSim simulation module. A: Endoscopy stack; B: Virtual reality views of the duodenum; C: Gastric cardia; D: Endoscope configuration.

evaluated over the 200 post-SPRINT procedures using generalised estimating equation (GEE) models, to account for the non-independence of repeated procedures by the same trainee. Prior to the analysis, the relationship between procedural experience and outcome measures were assessed graphically, and transformations applied, as applicable, to ensure goodness-of-fit. Binary logistic GEE models were then produced, using an autoregressive correlation structure. The trainee group (case/control) and the procedure number post-SPRINT were set as covariates, with an interaction term also included in the model. As such, the analysis allowed for the two groups to have different outcome rates at baseline, but also allowed for the rate of improvement over time to vary between the groups, with the interaction term allowing for comparison of the latter.

The times taken to reach the 200th procedure and for gastroscopy certification were assessed with Kaplan-Meier plots, with comparisons between cases and controls made using univariable Cox regression models. Trainees who did not achieve these outcomes were censored at the date of their final procedure. The procedure counts in the post-SPRINT period were then compared. To account for the potential loss of follow-up after gastroscopy certification, procedures performed after certification were excluded. Since this resulted in differing durations of follow up across the trainees, the total procedure counts were then divided by the time between the SPRINT course and gastroscopy certification, or to the final procedure date in those without certification, and analysed as an average number of procedures per month. All analyses were performed using SPSS v24 (IBM Corp. Armonk, NY), with $P < 0.05$ indicating statistical significance.

RESULTS

Participants

In total, 20 trainees and 6 faculty members (experts) attended the SPRINT induction programme. Of these, 10 trainees were classified as novices (< 25 procedures) and 10 as having intermediate experience (25+ procedures). Data from all participants were included in the analyses of EndoSim metrics and self-assessment scores. For the learning curve analyses, trainees were excluded on the basis of: Having no procedures recorded in the JETS e-portfolio (n = 3), > 50 pre-course procedures (n = 1), and first recorded procedure > 1 year before the course (n = 1), leaving 15 cases for analysis. Data for 24 control patients were identified. The majority of cases (93%) and controls (88%) were gastroenterology trainees, with upper gastrointestinal surgical trainees comprising the remainder. There were no significant differences in trainee specialty between groups (P = 0.967). Prior to the date of SPRINT, the average number of procedures performed was similar between the two groups (P = 0.739), with a mean of 10 per trainee in cases and 3 per trainee in controls; 63% of controls and 60% of cases had performed zero procedures prior to the course date.

Discriminative validity of EndoSim metrics

Comparisons of EndoSim metrics between trainees (novice and intermediate) and experts are presented in Table 2. Five gastroscopy-relevant modules were selected comprising: wheel handling, navigation, button handling, photodocumentation and biopsy, each with a variable number of substations. All trainees and faculty successfully completed and passed each station. Trainees could be differentiated from experts for at least one metric on all modules except for the "button handling" station. For the remaining stations, experts could be delineated from trainee performance in terms of efficiency metrics (*i.e.*, total time to complete a task), efficiency of movement (*e.g.*, more conservative wheel and scope rotation and less endoscope tip path length in the Navigation module, fewer collisions against the mucosa) and precision (fewer missed targets and more biopsies within target). Of the 22 metrics relevant to the five modules, 5 (23%) were significantly different between novice and intermediate trainees and 14 (64%) between trainees and experts.

Self-assessment scores

The 20 trainees attending SPRINT reported their confidence in 12 different skills both pre- and post-course. Across these skills, the median confidence score ranged from 3-5 on the pre-course questionnaire (Table 3). After the course, confidence in all 12 skills increased significantly (all P < 0.001), with medians ranging from 7-9.

Trends in procedural outcomes by course attendance

Preliminary analysis of the trends in unassisted D2 intubation rates found these to increase rapidly over the initial post-course procedures, with the rate of improvement slowing after 25-50 procedures and flattening subsequently as the D2 intubation rates neared 90%. Due to this rapid change in gradient, a binary logistic regression model with the lifetime procedure number as a covariate resulted in a poor fit. As such, lifetime procedure counts were $\log_2$-transformed, after adding 10, which improved the goodness-of-fit of the model.

This model was then applied to the cases and controls separately, using a GEE approach, to compare the rate of improvement between groups (Table 4, Figure 2A). This showed comparable baseline unassisted D2 intubation rates, with estimates of 28% for cases and 35% for controls at the first procedure post-SPRINT (P = 0.332). Unassisted D2 intubation rates improved with experience, with a doubling of the procedure count associated with an odds ratio of 1.99 in cases (P < 0.001) and 1.74 (P < 0.001) in controls (Table 4). However, no significant difference was detected between these gradients (P = 0.205). Hence, the rates of improvement in unassisted D2 intubation rates by procedure number were comparable between cases and controls.

Of the other outcomes considered, no significant differences in the rates of moderate-severe discomfort were detected between the case and control groups (Figure 2B). However, significant differences in the proportions of unsedated procedures were observed (Figure 2C). At baseline, the cases performed a significantly greater proportion of procedures without sedation (odds ratio: 1.63, 95%CI: 1.09–2.46, P = 0.018), with 58% of the first ten procedures by cases being unsedated, compared to 44% of those by controls. This difference between the groups was then sustained over the subsequent procedures (interaction term: P = 0.445).

Times to performance milestones

Over the post-SPRINT follow-up period of 16 mo, 13/15 (87%) cases and 15/24 (63%) controls reached a lifetime procedure count of 200. The Kaplan-Meier estimated median time to the 200th procedure (Figure 3A) did not differ significantly (P = 0.190) between cases (10.6 mo) and controls (12.1 mo). Gastroscopy certification was achieved in 11/15 (73%) cases and 7/24 controls (29%). Delegates achieved

Table 2 Comparisons of module-dependent EndoSim metrics between trainees (stratified into novice and intermediate experience groups) and faculty members

Module	Metric	Median (IQR)		*P* value (Expert *vs* trainee)	Median (IQR)		*P* value (Novice *vs* intermediate)
		Expert (*n* =6)	Trainee (*n* = 20)		Novice trainee (*n* = 10)	Intermediate trainee (*n* = 10)	
Module 1: Wheel Handling (4 stations)	**Missed targets**	3 (1-4)	6 (3-8)	**< 0.001**	7 (4-9)	6 (2-8)	0.057
	Wheel rotation left/right (Degrees)	257 (42-382)	143 (5-591)	0.463	82 (1-643)	166 (9-575)	0.753
	Wheel rotation up/down (Degrees)	783 (691-916)	764 (606-1173)	0.903	680 (442-1005)	1023 (687-1303)	**0.003**
	Endoscope rotation (Degrees)	1398 (749-2355)	964 (353-1577)	**0.025**	886 (350-1404)	1044 (349-1955)	0.350
Module 2: Navigation (3 stations)	**Total time (s)**	74 (52-104)	104 (79-166)	**0.002**	161 (108-218)	82 (67-105)	**< 0.001**
	Wheel rotation left/right (Degrees)	109 (40-305)	138 (3-757)	0.826	391 (3-1648)	99 (2-549)	0.143
	Wheel rotation up/down (Degrees)	888 (680-1108)	1232 (934-1868)	**0.001**	1268 (958-1737)	1224 (931-2046)	0.641
	Endoscope rotation (Degrees)	1120 (933-1865)	1770 (1313-2334)	**0.007**	1847 (1258-2571)	1722 (1357-2258)	0.503
	Endoscope tip path length (cm)	228 (179-306)	324 (251-411)	**0.002**	357 (280-489)	280 (239-356)	**0.028**
Module 3: Button Handling (3 stations)	**Missed targets (number)**	2 (0-4)	2 (1-4)	0.623	2 (1-5)	1.5 (1-4)	0.805
	Unnecessary button presses (number)	2 (0-4)	2 (1-4)	0.270	2 (1-5)	2 (1-4)	0.963
	Missed dirt (number)	1 (1-2)	1 (1-2)	0.944	1 (0-2)	1 (1-2)	0.429
Module 4: Photo (4 stations)	**Total time (s)**	151 (121-192)	313 (230-377)	**< 0.001**	328 (235-404)	269 (179-361)	0.054
	Stomach visualized (%)	93% (79%-99%)	100 (96%-100%)	**< 0.001**	99% (94%-100%)	100% (97%-100%)	0.070
	Duodenum visualized (%)	63% (52%-74%)	63% (53-72%)	0.855	62% (51%-68%)	66% (58%-74%)	0.088
	Collisions against mucosa (number)	8 (5-12)	13 (9-16)	**< 0.001**	13 (11-20)	12 (8-15)	0.090
	Targets photographed (%)	100% (100%-100%)	100% (100%-100%)	0.495	100% (100%-100%)	100% (100%-100%)	0.302
Module 5: Biopsy (3 stations)	**Total time (s)**	182 (163-217)	340 (249-463)	**< 0.001**	446 (331-522)	299 (215-389)	**0.001**
	Targets biopsied	100% (100%-100%)	100% (50-100%)	**0.010**	100% (38%-100%)	100% (50%-100%)	0.546
	Biopsies outside any target (number)	0 (0-2)	4 (2-9)	**< 0.001**	3 (2-8)	4 (2-11)	0.548
	Collisions against mucosa (number)	7 (4-11)	9 (7-13)	**0.030**	12 (9-23)	7 (6-11)	**< 0.001**
	Movement with tool (cm)	25 (17-53)	72 (36-183)	**0.002**	73 (29-183)	70 (42-179)	0.910

Data are presented as medians (interquartile ranges), with *P* values derived from Mann-Whitney tests. Bold *P* values are significant at $P < 0.05$. IQR: Interquartile ranges.

certification after a median time of 14 mo post-SPRINT, which was significantly earlier than controls (Figure 3B, $P = 0.017$), for whom the rate did not reach 50% (*i.e.*, the median time was > 16 mo). By the end of follow up (*i.e.*, 16 mo), the Kaplan-Meier estimated certification rates were 75% *vs* 36% in cases *vs* controls.

Table 3 Self-reported scores pre- and post-course

Skill	Median confidence score (IQR)		*P* value
	Pre-course	Post-course	
Tip control	5 (2-7)	8 (7-9)	**< 0.001**
Torque steering	5 (2-6)	8 (7-9)	**< 0.001**
Intubation	3 (0-7)	7 (6-9)	**< 0.001**
Oesophagus to pylorus	5 (1-8)	9 (7-9)	**< 0.001**
Pyloric intubation	4 (0-7)	8 (7-9)	**< 0.001**
D2 intubation	3 (0-6)	7 (5-9)	**< 0.001**
Duodenal withdrawal	4 (0-7)	8 (5-9)	**< 0.001**
J manoeuvre	5 (1-8)	8 (7-9)	**< 0.001**
Retroflexed views	5 (2-7)	8 (6-9)	**< 0.001**
Overall visualisation	5 (2-7)	8 (7-9)	**< 0.001**
Image taking	4 (1-6)	8 (7-8)	**< 0.001**
Use of accessories	3 (0-5)	8 (6-9)	**< 0.001**

Analysis is based on the n = 20 who attended the course. P values are from Wilcoxon's tests, with bold P values significant at $P < 0.05$. IQR: Interquartile range.

Post-course procedure counts

Cases performed a median of 16.2 (IQR: 13.8-20.8) procedures per month post-SPRINT, which was higher than the 13.8 (IQR: 9.2-16.7) observed in controls, although this missed statistical significance (P = 0.051).

DISCUSSION

In this small prospective case-control pilot study, trainees who attended a two-day hands-on gastroscopy induction course involving basic theory and SBT showed no significant difference in the learning curve to achieve unassisted D2 intubation. However, attenders achieved JAG certification earlier than peers from the control group, which may be explained by the tendency to perform more post-course procedures (P = 0.051). These results provide real-world data on the durability of an SBT induction programme on trainee and patient outcomes.

To account of the possibility of trainees attempting harder to complete an examination, discomfort and sedation-based outcomes were also explored. Course attenders performed more post-course procedures without sedation (P = 0.018), but without a significant difference in rates of moderate-severe discomfort (P = 0.090). To our knowledge, the only other publication which assessed the durability of SBT over 200 procedures was the randomised controlled trial (RCT) by Cohen *et al*[14] in the context of colonoscopy training. Trainees allocated to pre-clinical SBT demonstrated superior technical and cognitive outcomes during early stages of training, but this effect dissipated after 100 procedures. Previous RCTs on gastroscopy training have assessed post-SBT outcomes after 3-4 wk[15,16], or after 2-60 procedures of patient-based training[17-20], with the majority showing improvements in favour of SBT. Study protocols have also varied with regard to the duration of SBT exposure and training structure. Di Giulio *et al*[20] found that trainees randomised to 10 h of SBT performed better at unassisted D2 intubation, retroflexion and landmark identification over 20 patient-based procedures (88% *vs* 70%, $P < 0.001$). In another RCT, trainees who underwent 2 h of SBT demonstrated improved D2 intubation over 10 procedures, but no difference in patient discomfort scores[19].

Not all studies have associated SBT with improved outcomes. The Sedlack[16] study found no benefit in trainee gastroscopy outcomes after 6 h of SBT. Concerns over the face validity of the simulator was cited as a possible explanation. Our study presents novel evidence of discriminant validity of the EndoSim platform and response process validity in form of trainee feedback and the improvements in self-confidence scores. Although we found no significant difference between cases and controls in unassisted D2 intubation rates by procedure count, the rates at which trainees acquired competence, as evidenced by time-to-competency endpoints, was found in favour of SPRINT course attenders. It is recognised that coaching and feedback[8], coupled with a structured SBT curriculum[21], and a minimum exposure period to

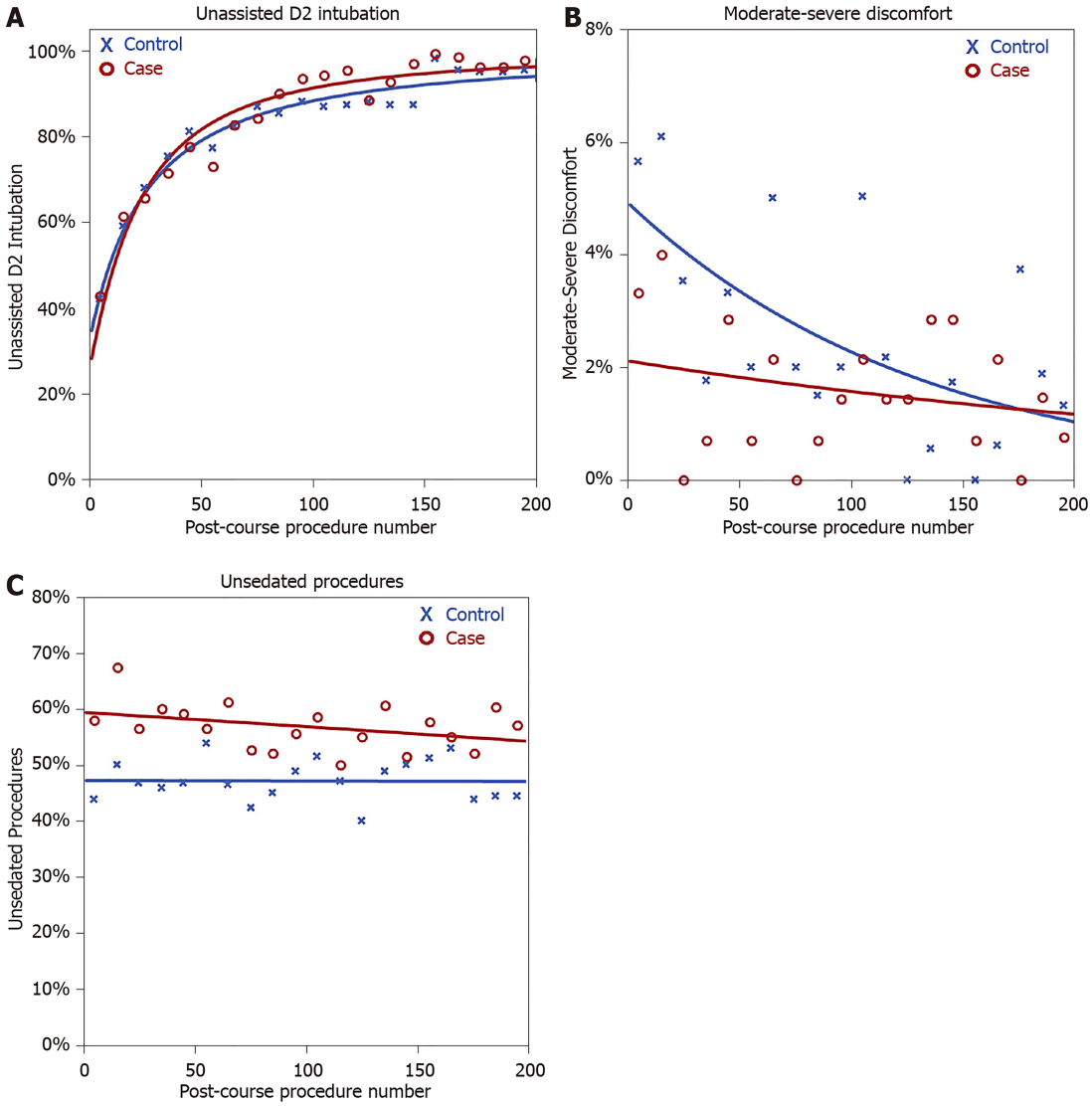

Figure 2 Plots of outcome rates by post-course procedure number, stratified according to cases and controls. A: Unassisted D2 intubation rates; B: Rates of moderate-severe discomfort; C: Unsedated procedures. Trendlines are extrapolated from generalised estimating equation models, as described in Table 4.

SBT[1], may be required to unlock the full potential of SBT. Notably, the difference between groups in rates of unsedated procedures may be another confounding factor.

Our study provides novel data from the perspective of UK-based endoscopy training which has its imperfections[4,22]. In addition to the lack of standardised SBT-curricula, training occurs within endoscopy units which face the perennial dilemma of balancing service capacity with list reductions to accommodate novice trainees. Trainees often face competing commitments, *e.g.*, from on-call rotas, ward and clinic duties, and may have to compete for training with other specialties[22]. It is possible that the improvements in trainee confidence derived from SPRINT may empower trainees to train on unsedated procedures and adopt a more proactive training stance, thereby leading to greater acquisition of training experience and shorter times to certification.

Our study had several noteworthy limitations. First, this was a non-randomised pilot study. Despite the similar numbers of pre-course procedures in the two groups, we cannot exclude differences in training provisions within the training regions for cases and controls. Second, this pilot study, with its 15 eligible cases, may be underpowered to detect statistically significant differences in long-term study outcomes. No formal power calculation was performed prior to study commencement, as the included trainees consisted of a convenience sample of SPRINT course attendees, hence there was no scope to increase the sample size. Third, not all trainees were fully novices, with approximately 40% having some degree of gastroscopy experience. However, this was generally limited to a small number of procedures and did not differ significantly between cases and controls. Fourth, the validity of EndoSim was not rigorously appraised, as the primary intention was to

Table 4 Generalised estimating equation models of procedure outcomes in cases and controls

	Cases		Controls		*P* value (Case *vs* Control)
	Odds ratio (95%CI)	*P* value	Odds ratio (95%CI)	*P* value	
Unassisted D2 intubation rates					
Intercept	0.51 (0.13 – 1.98)	-	-	-	0.332
Gradient (per Doubling of OGD count)	1.99 (1.69 – 2.34)	**< 0.001**	1.74 (1.53 – 1.98)	**< 0.001**	0.205
Moderate-severe discomfort					
Intercept	0.42 (0.15 - 1.15)	-	-	-	0.09
Gradient (per 10 procedures)	0.97 (0.88 - 1.07)	0.526	0.92 (0.85 - 1.00)	**0.044**	0.421
Unsedated procedures					
Intercept	1.63 (1.09 – 2.46)	-	-	-	**0.018**
Gradient (per 10 procedures)	0.99 (0.97 – 1.01)	0.28	1.00 (0.98 – 1.02)	0.973	0.445

Results are from generalised estimating equation models of the 200 procedures after the date of the course for each trainee. Each model contained the trainee group (case-control) and the procedure number as covariates, along with an interaction term. As such, the intercept represents the baseline difference between the case and control groups. The gradient represents the change in the outcome rate with increasing experience, with separate gradients reported for the case and control groups. For unassisted D2 rates, the procedure number was log-transformed in the model, hence the resulting coefficients were anti-logged, and gradients were reported per two-fold increase in procedure count. For the discomfort and unsedated procedures outcomes, gradients are reported per 10 additional procedures. The final column compares the gradients between groups, using the *P* value from the interaction term in the model. Bold *P* values are significant at $P < 0.05$.

provide training and to assess longer term outcomes. Further evaluation is required to appraise face validity, *i.e.*, realism, and comparisons of EndoSim performance over time. Fifth, owing to the comparisons of trainee and faculty performance of the EndoSim simulator, modules were initially performed by trainees without coaching or feedback, which are pivotal for skills acquisition with SBT. Faculty experts were unfamiliar to EndoSim and did not receive pre-course training. These factors may have compromised the effectiveness of hands-on technical skills training. Sixth, outcomes derived from the JETS e-portfolio is based on self-reported procedural data, which may be at risk of trainee selection bias. However, the outcome plots for both groups appear credible, and the use of JAG certification could be argued as a valid and objective endpoint. This limitation will be addressed with the upcoming integration of the National Endoscopy Database with the JETS e-portfolio, which will enable real-time and unbiased acquisition of lifetime procedure counts during endoscopy training[23]. Finally, the study assumed that trainees who logged procedures onto the JETS e-portfolio after the SPRINT date continued their training during the whole follow up period, and that all intended to reach the milestones of 200 procedures and OGD certification. As such, the analysis was performed on an "intention-to-treat" basis. We excluded trainees who performed no procedures after the date of SPRINT course, to remove those who did not pursue training. However, if there were trainees who ceased training subsequently or had prolonged breaks in training during follow-up, then these will remain included in the analysis, which may underestimate the outcomes measured.

In the face of the upcoming reforms to UK gastroenterology training[5], it is imperative for training programmes to ensure that endoscopy training has been sufficiently optimised. Our study shows that an induction programme for novices in endoscopy is feasible and implementable, can increase trainee confidence, and can shorten the time required to achieve competence for independent practice (JAG certification). Educators should evaluate the effect of educational interventions across training pathways to understand the longer-term outcomes of training. This pilot study provides promising data in support of augmented SBT induction, paving the way for larger and more robust future studies incorporating objective assessments of specific technical and non-technical skills[24], which will better determine its impact on trainee and patient outcomes.

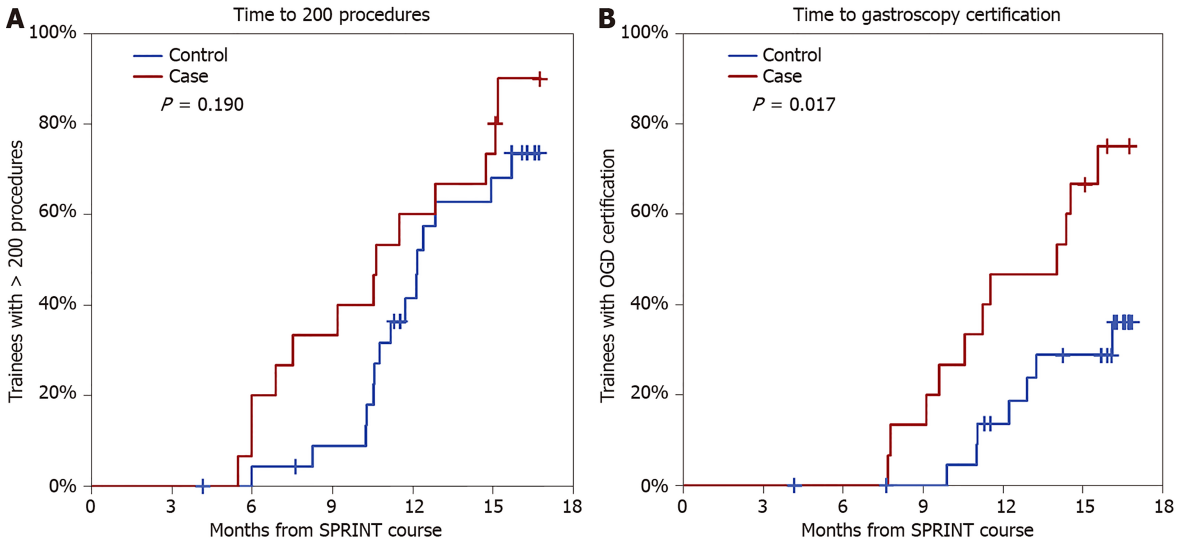

Figure 3 Kaplan-Meier curves of time to 200 procedures (A) and time to gastroscopy certification (B).

ARTICLE HIGHLIGHTS

Research background

Pre-clinical simulation-based training (SBT) in endoscopy has been shown to augment trainee performance in the short-term, but longer-term data are lacking. The EndoSim (Surgical Science, Gothenburg) is a novel endoscopic virtual reality simulator which incorporates a customisable SBT curriculum and generates task-specific metrics, but has not been validated.

Research motivation

In the United Kingdom, there is no standardised endoscopy SBT induction programme available prior to real-world, patient-based endoscopy training. The Structured PRogramme of INduction and Training (SPRINT) is a two-day gastroscopy induction course combining theory and SBT. We aimed to evaluate: (1) Whether the EndoSim simulator could differentiate between endoscopists of different experience (trainees *vs* experts); (2) Whether SPRINT improves trainee confidence in technical skills; and (3) Whether SPRINT impacted on longer term trainee outcomes.

Research methods

This prospective study had three components. First, computerised metrics generated by EndoSim were compared between trainees (n = 20) and experts (n = 6) to explore discriminative validity. Second, trainee feedback was acquired immediately pre- and post-course, and pairwise comparisons performed to assess impact of SPRINT on trainee confidence in technical skills. Third, a case-control study was performed to assess the impact of SPRINT on long-term outcomes (16-mo post-course period), which comprised: (1) Rates of unassisted procedural completion; (2) Post-course procedural exposure; (3) Procedural discomfort; (4) Sedation practice; and (5) Rates of gastroscopy certification. Controls matched for gastroscopy experience and study outcomes were derived from the United Kingdom training e-portfolio.

Research results

Of the modules relevant to gastroscopy training, a statistically significant difference was observed in 64% of EndoSIM metrics. Post-SPRINT, trainee confidence increased in all technical skills surveyed. For the case-control element, 15 cases and 24 controls were included, with mean procedure counts of 10 and 3 (P = 0.739) pre-SPRINT. Post-SPRINT, no significant differences between the groups were detected in long-term D2 intubation rates (P = 0.332) or discomfort scores (P = 0.090). However, the cases had a significantly higher rate of unsedated procedures than controls post-SPRINT (58% *vs* 44%, P = 0.018), which was maintained over the subsequent 200 procedures. Cases tended to perform procedures at a greater frequency than controls in the post-SPRINT period (median: 16.2 *vs* 13.8 per mo, P = 0.051), resulting in a significantly greater proportion of cases achieving gastroscopy certification by the end of follow up (75% *vs* 36%, P = 0.017).

Research conclusions

In this pilot study, attendees of the SPRINT cohort tended to perform more procedures and achieved gastroscopy certification earlier than controls, although no significant differences were shown in unassisted D2 intubation rates. These data support the role for wider evaluation of pre-clinical induction involving SBT.

Research perspectives

An induction programme for trainees in endoscopy is feasible and implementable, can increase trainee confidence, and can shorten the time required to achieve competence for independent practice (*i.e.*, certification). This pilot study provides promising data in support of augmented SBT induction, paving the way for phased implementation and larger real-world studies incorporating objective competency assessment tools to compare progress in specific technical and non-technical skills.

REFERENCES

1 **Siau K**, Hawkes ND, Dunckley P. Training in Endoscopy. *Curr Treat Options Gastroenterol* 2018; **16**: 345-361 [PMID: 30019105 DOI: 10.1007/s11938-018-0191-1]

2 **Siau K**, Green JT, Hawkes ND, Broughton R, Feeney M, Dunckley P, Barton JR, Stebbing J, Thomas-Gibson S. Impact of the Joint Advisory Group on Gastrointestinal Endoscopy (JAG) on endoscopy services in the UK and beyond. *Frontline Gastroenterol* 2019; **10**: 93-106 [PMID: 31210174 DOI: 10.1136/flgastro-2018-100969]

3 **Ward ST**, Hancox A, Mohammed MA, Ismail T, Griffiths EA, Valori R, Dunckley P. The learning curve to achieve satisfactory completion rates in upper GI endoscopy: an analysis of a national training database. *Gut* 2017; **66**: 1022-1033 [PMID: 26976733 DOI: 10.1136/gutjnl-2015-310443]

4 **Siau K**, Anderson JT, Valori R, Feeney M, Hawkes ND, Johnson G, McKaig BC, Pullan RD, Hodson J, Wells C, Thomas-Gibson S, Haycock AV, Beales ILP, Broughton R, Dunckley P; Joint Advisory Group on Gastrointestinal Endoscopy (JAG). Certification of UK gastrointestinal endoscopists and variations between trainee specialties: results from the JETS e-portfolio. *Endosc Int Open* 2019; **7**: E551-E560 [PMID: 30957005 DOI: 10.1055/a-0839-4476]

5 **Clough J**, FitzPatrick M, Harvey P, Morris L. Shape of Training Review: an impact assessment for UK gastroenterology trainees. *Frontline Gastroenterol* 2019; **10**: 356-363 [PMID: 31656560 DOI: 10.1136/flgastro-2018-101168]

6 **Qiao W**, Bai Y, Lv R, Zhang W, Chen Y, Lei S, Zhi F. The effect of virtual endoscopy simulator training on novices: a systematic review. *PLoS One* 2014; **9**: e89224 [PMID: 24586609 DOI: 10.1371/journal.pone.0089224]

7 **Singh S**, Sedlack RE, Cook DA. Effects of simulation-based training in gastrointestinal endoscopy: a systematic review and meta-analysis. *Clin Gastroenterol Hepatol* 2014; **12**: 1611-23.e4 [PMID: 24509241 DOI: 10.1016/j.cgh.2014.01.037]

8 **Khan R**, Plahouras J, Johnston BC, Scaffidi MA, Grover SC, Walsh CM. Virtual reality simulation training for health professions trainees in gastrointestinal endoscopy. *Cochrane Database Syst Rev* 2018; **8**: CD008237 [PMID: 30117156 DOI: 10.1002/14651858.CD008237.pub3]

9 **Siau K**, Hodson J, Valori RM, Ward ST, Dunckley P. Performance indicators in colonoscopy after certification for independent practice: outcomes and predictors of competence. *Gastrointest Endosc* 2019; **89**: 482-492.e2 [PMID: 30076842 DOI: 10.1016/j.gie.2018.07.032]

10 **Vassiliou MC**, Dunkin BJ, Fried GM, Mellinger JD, Trus T, Kaneva P, Lyons C, Korndorffer JR, Ujiki M, Velanovich V, Kochman ML, Tsuda S, Martinez J, Scott DJ, Korus G, Park A, Marks JM. Fundamentals of endoscopic surgery: creation and validation of the hands-on test. *Surg Endosc* 2014; **28**: 704-711 [PMID: 24253562 DOI: 10.1007/s00464-013-3298-4]

11 **Mehta T**, Dowler K, McKaig BC, Valori RM, Dunckley P. Development and roll out of the JETS e-portfolio: a web based electronic portfolio for endoscopists. *Frontline Gastroenterol* 2011; **2**: 35-42 [PMID: 28839580 DOI: 10.1136/fg.2010.003269]

12 **Siau K**, Crossley J, Dunckley P, Johnson G, Feeney M, Hawkes ND, Beales ILP; Joint Advisory Group on Gastrointestinal Endoscopy (JAG). Direct observation of procedural skills (DOPS) assessment in diagnostic gastroscopy: nationwide evidence of validity and competency development during training. *Surg Endosc* 2020; **34**: 105-114 [PMID: 30911922 DOI: 10.1007/s00464-019-06737-7]

13 **Siau K**, Dunckley P, Valori R, Feeney M, Hawkes ND, Anderson JT, Beales ILP, Wells C, Thomas-Gibson S, Johnson G; Joint Advisory Group on Gastrointestinal Endoscopy (JAG). Changes in scoring of Direct Observation of Procedural Skills (DOPS) forms and the impact on competence assessment. *Endoscopy* 2018; **50**: 770-778 [PMID: 29614526 DOI: 10.1055/a-0576-6667]

14 **Cohen J**, Cohen SA, Vora KC, Xue X, Burdick JS, Bank S, Bini EJ, Bodenheimer H, Cerulli M, Gerdes H, Greenwald D, Gress F, Grosman I, Hawes R, Mullin G, Schnoll-Sussman F, Starpoli A, Stevens P, Tenner S, Villanueva G. Multicenter, randomized, controlled trial of virtual-reality simulator training in acquisition of competency in colonoscopy. *Gastrointest Endosc* 2006; **64**: 361-368 [PMID: 16923483 DOI: 10.1016/j.gie.2005.11.062]

15 **Ferlitsch A**, Glauninger P, Gupper A, Schillinger M, Haefner M, Gangl A, Schoefl R. Evaluation of a virtual endoscopy simulator for training in gastrointestinal endoscopy. *Endoscopy* 2002; **34**: 698-702 [PMID: 12195326 DOI: 10.1055/s-2002-33456]

16 **Sedlack RE**. Validation of computer simulation training for esophagogastroduodenoscopy: Pilot study. *J Gastroenterol Hepatol* 2007; **22**: 1214-1219 [PMID: 17559386 DOI: 10.1111/j.1440-1746.2007.04841.x]

17 **Shirai Y**, Yoshida T, Shiraishi R, Okamoto T, Nakamura H, Harada T, Nishikawa J, Sakaida I. Prospective randomized study on the use of a computer-based endoscopic simulator for training in esophagogastroduodenoscopy. *J Gastroenterol Hepatol* 2008; **23**: 1046-1050 [PMID: 18554236 DOI: 10.1111/j.1440-1746.2008.05457.x]

18 **Ende A**, Zopf Y, Konturek P, Naegel A, Hahn EG, Matthes K, Maiss J. Strategies for training in diagnostic upper endoscopy: a prospective, randomized trial. *Gastrointest Endosc* 2012; **75**: 254-260 [PMID: 22153875 DOI: 10.1016/j.gie.2011.07.063]

19 **Ferlitsch A**, Schoefl R, Puespoek A, Miehsler W, Schoeniger-Hekele M, Hofer H, Gangl A, Homoncik M. Effect of virtual endoscopy simulator training on performance of upper gastrointestinal endoscopy in patients: a randomized controlled trial. *Endoscopy* 2010; **42**: 1049-1056 [PMID: 20972956 DOI: 10.1055/s-0030-1255818]

20 **Di Giulio E**, Fregonese D, Casetti T, Cestari R, Chilovi F, D'Ambra G, Di Matteo G, Ficano L, Delle Fave G. Training with a computer-based simulator achieves basic manual skills required for upper endoscopy: a randomized controlled trial. *Gastrointest Endosc* 2004; **60**: 196-200 [PMID: 15278044 DOI: 10.1016/s0016-5107(04)01566-4]

21 **Grover SC**, Scaffidi MA, Khan R, Garg A, Al-Mazroui A, Alomani T, Yu JJ, Plener IS, Al-Awamy M, Yong EL, Cino M, Ravindran NC, Zasowski M, Grantcharov TP, Walsh CM. Progressive learning in endoscopy simulation training improves clinical performance: a blinded randomized trial. *Gastrointest Endosc* 2017; **86**: 881-889 [PMID: 28366440 DOI: 10.1016/j.gie.2017.03.1529]

22 **Biswas S**, Alrubaiy L, China L; British Society of Gastroenterology Trainees' Section, Lockett M, Ellis A, Hawkes N. Trends in UK endoscopy training in the BSG trainees' national survey and strategic planning for the future. *Frontline Gastroenterol* 2018; **9**: 200-207 [PMID: 30046424 DOI: 10.1136/flgastro-2017-100848]

23 **Lee TJ**, Siau K, Esmaily S, Docherty J, Stebbing J, Brookes MJ, Broughton R, Rogers P, Dunckley P, Rutter MD. Development of a national automated endoscopy database: The United Kingdom National Endoscopy Database (NED). *United European Gastroenterol J* 2019; **7**: 798-806 [PMID: 31316784 DOI: 10.1177/2050640619841539]

24 **Siau K**, Kuwai T, Ishaq S. Analysis of learning curves in gastroscopy training: the need for composite measures for defining competence. *Gut* 2018; **67**: 1198 [PMID: 28814483 DOI: 10.1136/gutjnl-2017-314954]

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CASE REPORT

Gallbladder perforation due to endoscopic sleeve gastroplasty: A case report and review of literature

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Author contributions: de Moura DTH and Barrichello SA conceived and designed the study; de Siqueira Neto J performed the procedure; Ribeiro IB carried out the literature search; Harthorn KE and Thompson CC reviewed the case and edited the manuscript; all authors contributed to finalizing the present version of the paper and approved the manuscript for publication.

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Abstract

BACKGROUND

The healthcare impact of obesity is enormous, and there have been calls for new approaches to containing the epidemic worldwide. Minimally invasive procedures have become more popular, with one of the most widely used being endoscopic sleeve gastroplasty (ESG). Although major adverse events after ESG are rare, some can cause considerable mortality. To our knowledge, there has been no previous report of biliary ascites after ESG.

CASE SUMMARY

A 48-year-old female with obesity refractory to lifestyle changes and prior gastric balloon placement underwent uncomplicated ESG and was discharged on the following day. On postoperative day 3, she developed abdominal pain, which led to an emergency department visit the following day. She was readmitted to the hospital, with poor general health status and signs of peritoneal irritation. Computed tomography imaging showed fluid in the abdominal cavity. Laparoscopy revealed biliary ascites and showed that the gallbladder was sutured to the gastric wall. The patient underwent cholecystectomy and lavage of the abdominal cavity and was admitted to the intensive care unit post-operatively. After 7 d of antibiotic therapy and 20 d of hospitalization, she was discharged. Fortunately, 6 mo later, she presented in excellent general condition and with a 20.2% weight loss.

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CONCLUSION
ESG is a safe procedure. However, adverse events can still occur, and precautions should be taken by the endoscopist. In general, patient position, depth of tissue acquisition, location of stitch placement, and endoscopist experience are all important factors to consider to mitigate procedural risk.

Key words: Bariatric surgery; Obesity; Weight loss; Peritonitis; Case report

Core tip: Despite broader acceptance of endoscopic sleeve gastroplasty for weight loss management, the procedure can still present challenges for endoscopists. Although the inadvertent puncture of organs adjacent to the stomach is a rare occurrence, it can lead to catastrophic outcomes. Early identification of possible unintended events and an assertive approach to case management can be life-saving. Patient selection and optimal technique remain under debate. With broader adoption of endoscopic sleeve gastroplasty worldwide, risk mitigation strategies must be emphasized to optimize procedural safety.

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INTRODUCTION

Obesity is a disease of great social and financial impact which can lead to significant health conditions, such as cardiovascular disease, non-alcoholic steatohepatitis, osteoarthritis, obstructive sleep apnea, depression, and gastroesophageal reflux disease[1-3]. In recent years, endoscopic procedures have begun to fill the large gap between medical and surgical treatments aimed at controlling this disease[4,5]. One of the recently developed procedures is endoscopic sleeve gastroplasty (ESG), which is performed with a suturing device coupled to the distal tip of an endoscope enabling placement of full thickness sutures in the gastric wall to alter the form and function of the stomach.

Although ESG is considered to be a safe procedure[6-8], various major and minor adverse events have been described[9]. According to previous studies, the most common symptoms occurring after ESG are nausea, vomiting, and mild-to-moderate abdominal pain[9-11]. Severe adverse events, such as peritoneal fluid collections requiring drainage or surgical intervention, gastrointestinal or intraabdominal hemorrhage requiring intervention or transfusion, or severe abdominal pain are rare, occurring in only 0-2% of reported cases[9-12].

To our knowledge, only one prior case of biliary peritonitis during ESG has been reported[13], however, ascites was not described in this case. Our case of gallbladder perforation and biliary ascites was identified early and appropriately managed leading to a favorable outcome for the patient, similar to the aforementioned case. Given the rapid increase in the number of ESG procedures worldwide, it is imperative to document and educate one another on adverse events to reduce their rate of occurrence and minimize the morbidity associated with the procedure.

CASE PRESENTATION

Chief complaint

A 48-year-old female with obesity and with various comorbidities.

History of present illness

A 48-year-old female with obesity was referred for consideration of ESG. She had a medical history significant for hypertension that was controlled with oral agents. She had no prior history of bariatric surgery. At initial presentation, her weight was 93 kg, with a body mass index of 31.4 kg/m^2, despite lifestyle changes and prior placement

of a gastric balloon.

The patient gave written informed consent, after which she underwent ESG at a private hospital (Hospital Meridional, Cariacica, ES, Brazil). This was the first ESG performed at this center. There were no immediate procedural related complications. The procedure was performed under general anesthesia, with an endoscopic suturing system (OverStitch endosuturing device; Apollo Endosurgery, Austin, TX, United States) coupled to a dual-channel endoscope (GIF-2T160; Olympus America, Center Valley, PA, United States). Carbon dioxide insufflation was used. A full thickness U-shaped suture pattern was used by the physician to perform ESG, as previously described[10] (Figure 1). A total of five sutures were used.

In the immediate postoperative period, the patient was treated daily with antiemetics (ondansetron, dimenhydrinate, dexamethasone, and scopolamine), as well as dipyrone and omeprazole. The patient was discharged on post-operative day 1, in good condition and without any complaints, with prescriptions for omeprazole, ondansetron, dipyrone, scopolamine, and codeine phosphate combined with acetaminophen if necessary.

On postoperative day 3, the patient developed abdominal pain which continued to worsen over the next 24 h; thus, she was referred to the emergency department for further evaluation.

History of past illness

Obesity and hypertension.

Physical examination

Physical examination was normal preoperatively. On the fourth postoperative day, the patient had a rigid abdomen with signs of peritoneal irritation.

Laboratory examinations

On the fourth postoperative day and admission to the emergency department, the patient had significant leukocytosis (19800 × 103 leukocytes/μL) and an increased C-reactive protein level (147 mg/L).

Imaging examinations

At the emergency entrance, computed tomography imaging revealed free fluid in the peritoneal cavity (Figure 2).

FINAL DIAGNOSIS

The patient was diagnosed with biliary ascites caused by inadvertent puncture of the gallbladder.

TREATMENT

Patient was taken for emergent diagnostic laparoscopy. In addition to the biliary ascites, the stomach appeared to be tubular in shape as expected post-ESG. After significant lavage of the peritoneal cavity, it was noted that the fundus of the gallbladder was transfixed to the stomach (Figure 3). Biliary fluid collections were identified throughout the upper abdomen (Figure 4). Thus, the suture was cut and laparoscopic cholecystectomy was performed. At the conclusion of the case, intraoperative endoscopy with a methylene blue test was performed, finding no evidence of additional complications.

OUTCOME AND FOLLOW-UP

The patient was admitted to the intensive care unit, where she remained for one week, requiring IV antibiotics for septic shock. She did not require further surgical intervention. She ultimately improved from an infectious perspective, and was discharged to home 20 d after her initial admission to the hospital.

At the time of this case report (Table 1), the patient continued to follow in the outpatient clinic, and had no further complications related to the procedure. She had lost 18.7 kg (20.2% of her total body weight) in the first six months after the ESG. She was still undergoing interdisciplinary follow-up with a nutritionist, a psychologist, and a physical therapist.

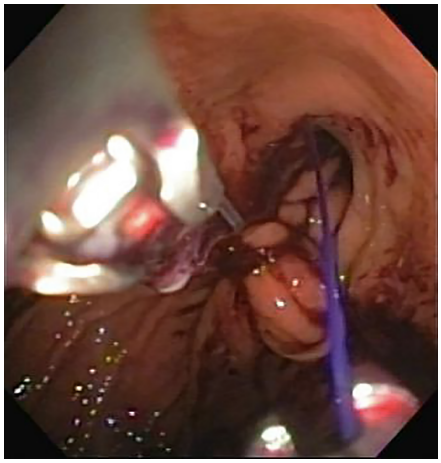

Figure 1 Endoscopic suture placement during endoscopic sleeve.

DISCUSSION

Endoscopic treatment of obesity has begun to rapidly fill the gap between medical and surgical therapies, as endoscopic therapy provides a minimally invasive option, which has greater efficiency than medical interventions and a greater safety profile than open surgical interventions[14-17]. The advent of endoscopic suturing was a major step forward in the minimally invasive treatment of a number of gastrointestinal pathologies[18,19]. The OverStitch Endosuturing device has stood out from other such systems and is currently the only system in widespread use[8]. Since 2001, endoscopic suturing systems have been adapted for the treatment of obesity, as experiments in *ex vivo* animal models have led to the development of the systems and techniques in use today[20]. In ESG, full thickness sutures are placed throughout the gastric body to bring the anterior wall, greater curvature, and posterior wall of the gastric body all closer together, resulting in a tubular configuration[8], in a manner similar to that achieved with surgical sleeve gastrectomy. The technique has been improving since 2012, when Thompson and Hawes performed the first ESG[11,21]. Since then, Abu Dayyeh *et al*[22] and Sharaiha *et al*[23] confirmed the technical feasibility of the procedure, as well as its safety and efficacy for weight reduction.

Minor adverse events, such as nausea, vomiting, and mild-to-moderate abdominal pain are the most common symptoms following ESG. In a study involving 1000 patients whom underwent ESG, Alqahtani *et al*[10] observed minor adverse events in 92.2% of patients. However, while there were high rates of minor adverse events reported, there were very few major adverse events associated with the procedure[10]. A recently published review article on the topic by Jain *et al*[24] evaluated nine original articles and confirmed that there was a high incidence of minor adverse events, while similarly demonstrated a low rate of major adverse events, seen only in 2.3% of cases. Of note, there was no incidence of biliary injury or ascites described in this analysis.

Despite an exhaustive search of the literature, we found no reports of death related to the procedure. Readmissions due to upper gastrointestinal hemorrhage requiring endoscopic intervention or administration of blood products occur only occasionally, having a minimal impact on morbidity and length of hospital stay[10,25]. Among the major adverse events occurring after ESG, leaks and peritoneal fluid collections are most common, having been reported in various studies in the literature[7,10,11,25-30]. In most cases, the complication was treated conservatively or by image-guided percutaneous drainage.

On detailed review of this case, there were several factors that may have contributed to this adverse event. There is a learning curve associated with any endoscopic procedure, including ESG, and this case was the very first ESG performed by the endoscopist. Despite this procedure being performed under the supervision of an experienced proctor, this may have contributed. Additionally, the patient was in the "swimmers" position, instead of a more conventional supine, lazy left-lateral position, which may have brought the stomach and gallbladder into closer proximity, thus increasing the risk of gallbladder perforation with a full-thickness gastric suturing technique. And finally, we believe that the suturing was started in close proximity to the lesser curvature of the stomach, which could have also increased the risk of biliary injury.

As described in this case report, biliary ascites after ESG should be considered as a

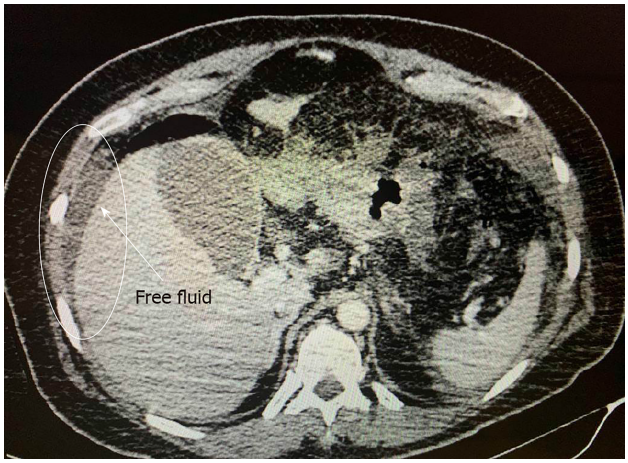

Figure 2 Computerized tomography showing free fluid in the abdominal cavity.

rare but major adverse event of great clinical severity. The treatment team must maintain a high level of diagnostic suspicion in a patient presenting with fever and abdominal pain following ESG. Timely, aggressive therapy must be taken to minimize long term sequelae.

CONCLUSION

Although rare, gallbladder perforation can occur during ESG, and can have significant clinical consequences. Further studies, focusing on patient positioning, use of anatomic landmarks to guide suture patterns, and learning curve should be performed to further reduce the occurrence of adverse events such as the one described here.

Table 1 Case report time line

Time line	
1	Patient underwent endoscopic sleeve gastroplasty with no complications
2	On postoperative day 3, she developed abdominal pain, which led to an emergency department visit on postoperative day
3	She was readmitted to the hospital, with poor general health status and signs of peritoneal irritation
4	Computed tomography showed fluid in the abdominal cavity
5	Laparoscopy revealed biliary ascites and showed that the gallbladder was sutured to the gastric wall
6	The patient underwent cholecystectomy, together with review and lavage of the abdominal cavity, and was admitted to the intensive care unit
7	After 7 d of antibiotic therapy and 20 d of hospitalization, she was discharged
8	Of 6 mo later, she presented excellent general condition and a 20.2% weight loss

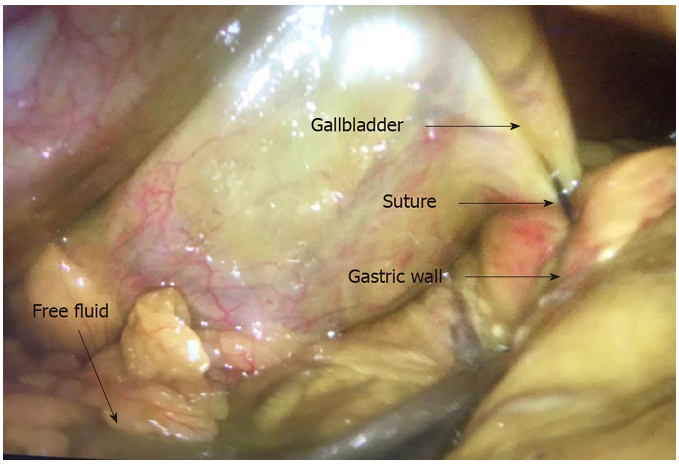

Figure 3 Laparoscopic visualization showing bile ascites, the gallbladder, the stomach, and a suture between the gallbladder and the stomach.

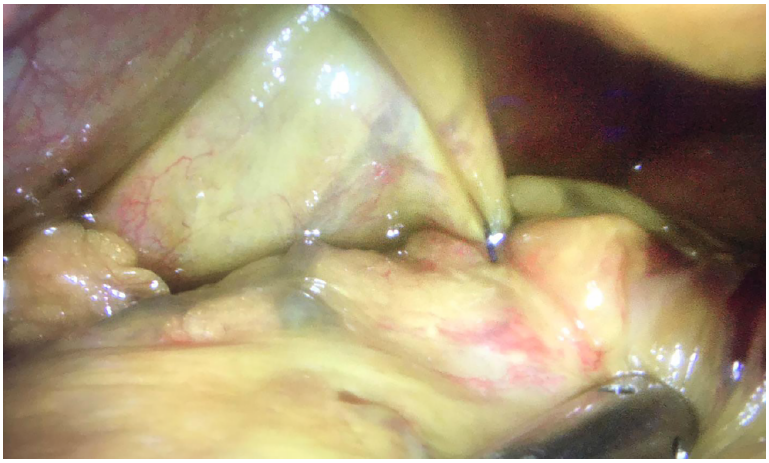

Figure 4 Laparoscopic visualization of a suture in the gallbladder after aspiration of bile ascites.

REFERENCES

1 **GBD 2015 Obesity Collaborators**. Afshin A, Forouzanfar MH, Reitsma MB, Sur P, Estep K, Lee A, Marczak L, Mokdad AH, Moradi-Lakeh M, Naghavi M, Salama JS, Vos T, Abate KH, Abbafati C, Ahmed MB, Al-Aly Z, Alkerwi A, Al-Raddadi R, Amare AT, Amberbir A, Amegah AK, Amini E, Amrock SM, Anjana RM, Ärnlöv J, Asayesh H, Banerjee A, Barac A, Baye E, Bennett DA, Beyene AS, Biadgilign S, Biryukov S, Bjertness E, Boneya DJ, Campos-Nonato I, Carrero JJ, Cecilio P, Cercy K, Ciobanu LG, Cornaby L, Damtew SA, Dandona L, Dandona R, Dharmaratne SD, Duncan BB, Eshrati B, Esteghamati A, Feigin VL, Fernandes JC, Fürst T, Gebrehiwot TT, Gold A, Gona PN, Goto A, Habtewold TD, Hadush KT, Hafezi-Nejad N, Hay SI, Horino M, Islami F, Kamal R, Kasaeian A, Katikireddi SV, Kengne AP, Kesavachandran CN, Khader YS, Khang YH, Khubchandani J, Kim D, Kim YJ, Kinfu Y, Kosen S, Ku T,

Defo BK, Kumar GA, Larson HJ, Leinsalu M, Liang X, Lim SS, Liu P, Lopez AD, Lozano R, Majeed A, Malekzadeh R, Malta DC, Mazidi M, McAlinden C, McGarvey ST, Mengistu DT, Mensah GA, Mensink GBM, Mezgebe HB, Mirrakhimov EM, Mueller UO, Noubiap JJ, Obermeyer CM, Ogbo FA, Owolabi MO, Patton GC, Pourmalek F, Qorbani M, Rafay A, Rai RK, Ranabhat CL, Reinig N, Safiri S, Salomon JA, Sanabria JR, Santos IS, Sartorius B, Sawhney M, Schmidhuber J, Schutte AE, Schmidt MI, Sepanlou SG, Shamsizadeh M, Sheikhbahaei S, Shin MJ, Shiri R, Shiue I, Roba HS, Silva DAS, Silverberg JI, Singh JA, Stranges S, Swaminathan S, Tabarés-Seisdedos R, Tadese F, Tedla BA, Tegegne BS, Terkawi AS, Thakur JS, Tonelli M, Topor-Madry R, Tyrovolas S, Ukwaja KN, Uthman OA, Vaezghasemi M, Vasankari T, Vlassov VV, Vollset SE, Weiderpass E, Werdecker A, Wesana J, Westerman R, Yano Y, Yonemoto N, Yonga G, Zaidi Z, Zenebe ZM, Zipkin B, Murray CJL. Health Effects of Overweight and Obesity in 195 Countries over 25 Years. *N Engl J Med* 2017; **377**: 13-27 [PMID: 28604169 DOI: 10.1056/NEJMoa1614362]

2 **Hourneaux De Moura DT**, Thompson CC. Endoscopic management of weight regain following Roux-en-Y gastric bypass. *Expert Rev Endocrinol Metab* 2019; **14**: 97-110 [PMID: 30691326 DOI: 10.1080/17446651.2019.1571907]

3 **Ribeiro IB**, Gestic MA, Utrini MP, Chaim FDM, Chaim EA, Cazzo E. Drain amylase levels may indicate gastrojejunostomy leaks after roux-en-y gastric bypass. *Arq Gastroenterol* 2018; **55**: 66-72 [PMID: 29561980 DOI: 10.1590/S0004-2803.201800000-13]

4 **de Almeida LS**, Bazarbashi AN, de Souza TF, de Moura BFBH, de Moura DTH. Modifying an Intragastric Balloon for the Treatment of Obesity: a Unique Approach. *Obes Surg* 2019; **29**: 1445-1446 [PMID: 30737762 DOI: 10.1007/s11695-019-03771-1]

5 **de Moura DTH**, de Moura EGH, Neto MG, Thompson CC. To the Editor. *Surg Obes Relat Dis* 2019; **15**: 155-157 [PMID: 30477752 DOI: 10.1016/j.soard.2018.10.006]

6 **Lopez-Nava G**, Galvão MP, Bautista-Castaño I, Fernandez-Corbelle JP, Trell M, Lopez N. Endoscopic sleeve gastroplasty for obesity treatment: two years of experience. *Arq Bras Cir Dig* 2017; **30**: 18-20 [PMID: 28489162 DOI: 10.1590/0102-6720201700010006]

7 **Sartoretto A**, Sui Z, Hill C, Dunlap M, Rivera AR, Khashab MA, Kalloo AN, Fayad L, Cheskin LJ, Marinos G, Wilson E, Kumbhari V. Endoscopic Sleeve Gastroplasty (ESG) Is a Reproducible and Effective Endoscopic Bariatric Therapy Suitable for Widespread Clinical Adoption: a Large, International Multicenter Study. *Obes Surg* 2018; **28**: 1812-1821 [PMID: 29450845 DOI: 10.1007/s11695-018-3135-x]

8 **de Moura DTH**, de Moura EGH, Thompson CC. Endoscopic sleeve gastroplasty: From whence we came and where we are going. *World J Gastrointest Endosc* 2019; **11**: 322-328 [PMID: 31205593 DOI: 10.4253/wjge.v11.i5.322]

9 **Lopez-Nava G**, Sharaiha RZ, Vargas EJ, Bazerbachi F, Manoel GN, Bautista-Castaño I, Acosta A, Topazian MD, Mundi MS, Kumta N, Kahaleh M, Herr AM, Shukla A, Aronne L, Gostout CJ, Abu Dayyeh BK. Endoscopic Sleeve Gastroplasty for Obesity: a Multicenter Study of 248 Patients with 24 Months Follow-Up. *Obes Surg* 2017; **27**: 2649-2655 [PMID: 28451929 DOI: 10.1007/s11695-017-2693-7]

10 **Alqahtani A**, Al-Darwish A, Mahmoud AE, Alqahtani YA, Elahmedi M. Short-term outcomes of endoscopic sleeve gastroplasty in 1000 consecutive patients. *Gastrointest Endosc* 2019; **89**: 1132-1138 [PMID: 30578757 DOI: 10.1016/j.gie.2018.12.012]

11 **Barrichello S**, Hourneaux de Moura DT, Hourneaux de Moura EG, Jirapinyo P, Hoff AC, Fittipaldi-Fernandez RJ, Baretta G, Felício Lima JH, Usuy EN, de Almeida LS, Ramos FM, Matz F, Galvão Neto MDP, Thompson CC. Endoscopic sleeve gastroplasty in the management of overweight and obesity: an international multicenter study. *Gastrointest Endosc* 2019; **90**: 770-780 [PMID: 31228432 DOI: 10.1016/j.gie.2019.06.013]

12 **Kumar N**, Sahdala HNP, Shaikh S, Wilson EB, Manoel GN, Zundel N, Thompson CC. Mo1155 Endoscopic Sleeve Gastroplasty for Primary Therapy of Obesity: Initial Human Cases. *Gastroenterology* 2014; **146**: S-571-S-572 [DOI: 10.1016/S0016-5085(14)62071-0]

13 **Lopez-Nava G**, Asokkumar R, Ielpo B, Bautista I, Vicente E. Biliary peritonitis after endoscopic sutured gastroplasty for morbid obesity (with video). *Gastrointest Endosc* 2019; **90**: 686-688 [PMID: 31375266 DOI: 10.1016/j.gie.2019.06.002]

14 **Genco A**, Cipriano M, Materia A, Bacci V, Maselli R, Musmeci L, Lorenzo M, Basso N. Laparoscopic sleeve gastrectomy versus intragastric balloon: a case-control study. *Surg Endosc* 2009; **23**: 1849-1853 [PMID: 19169745 DOI: 10.1007/s00464-008-0285-2]

15 **Moura D**, Oliveira J, De Moura EG, Bernardo W, Galvão Neto M, Campos J, Popov VB, Thompson C. Effectiveness of intragastric balloon for obesity: A systematic review and meta-analysis based on randomized control trials. *Surg Obes Relat Dis* 2016; **12**: 420-429 [PMID: 26968503 DOI: 10.1016/j.soard.2015.10.077]

16 **Baptista A**, Hourneaux De Moura DT, Jirapinyo P, Hourneaux De Moura EG, Gelrud A, Kahaleh M, Salinas A, Sabagh LC, Ospina A, Rincones VZ, Doval R, Bandel JW, Thompson CC. Efficacy of the cardiac septal occluder in the treatment of post-bariatric surgery leaks and fistulas. *Gastrointest Endosc* 2019; **89**: 671-679.e1 [PMID: 30529441 DOI: 10.1016/j.gie.2018.11.034]

17 **de Moura DTH**, Ribeiro IB, Funari MP, Baptista A, Thompson CC, de Moura EGH. Novel use of a cardiac septal occluder to treat a chronic recalcitrant bariatric fistula after Roux-en-Y gastric bypass. *Endoscopy* 2019; **51**: E111-E112 [PMID: 30791049 DOI: 10.1055/a-0842-6287]

18 **Halvax P**, Diana M, Nagao Y, Marescaux J, Swanström L. Experimental Evaluation of the Optimal Suture Pattern With a Flexible Endoscopic Suturing System. *Surg Innov* 2017; **24**: 201-204 [PMID: 28492354 DOI: 10.1177/1553350617697184]

19 **Madruga-Neto AC**, Bernardo WM, de Moura DTH, Brunaldi VO, Martins RK, Josino IR, de Moura ETH, de Souza TF, Santo MA, de Moura EGH. The Effectiveness of Endoscopic Gastroplasty for Obesity Treatment According to FDA Thresholds: Systematic Review and Meta-Analysis Based on Randomized Controlled Trials. *Obes Surg* 2018; **28**: 2932-2940 [PMID: 29909512 DOI: 10.1007/s11695-018-3335-4]

20 **Awan AN**, Swain CP. Endoscopic vertical band gastroplasty with an endoscopic sewing machine. *Gastrointest Endosc* 2002; **55**: 254-256 [PMID: 11818935 DOI: 10.1067/mge.2002.120889]

21 **Neto MG**, Zundel N, Campos J, Alvarado A, Silva L, Orilaac J, Shaikh S, Gomez E, Wilson E, Thompson CC. ET010 Endoluminal greater curvature plication-A case series. SAGES. Available from: https://www.sages.org/meetings/annual-meeting/abstracts-archive/endoluminal-greater-curvature-plication-a-case-series/

22 **Abu Dayyeh BK**, Rajan E, Gostout CJ. Endoscopic sleeve gastroplasty: a potential endoscopic alternative to surgical sleeve gastrectomy for treatment of obesity. *Gastrointest Endosc* 2013; **78**: 530-535 [PMID:

23711556 DOI: 10.1016/j.gie.2013.04.197]
23 **Sharaiha RZ**, Kedia P, Kumta N, DeFilippis EM, Gaidhane M, Shukla A, Aronne LJ, Kahaleh M. Initial experience with endoscopic sleeve gastroplasty: technical success and reproducibility in the bariatric population. *Endoscopy* 2015; **47**: 164-166 [PMID: 25380510 DOI: 10.1055/s-0034-1390773]
24 **Jain D**, Bhandari BS, Arora A, Singhal S. Endoscopic Sleeve Gastroplasty - A New Tool to Manage Obesity. *Clin Endosc* 2017; **50**: 552-561 [PMID: 28607328 DOI: 10.5946/ce.2017.032]
25 **Fayad L**, Adam A, Schweitzer M, Cheskin LJ, Ajayi T, Dunlap M, Badurdeen DS, Hill C, Paranji N, Lalezari S, Kalloo AN, Khashab MA, Kumbhari V. Endoscopic sleeve gastroplasty versus laparoscopic sleeve gastrectomy: a case-matched study. *Gastrointest Endosc* 2019; **89**: 782-788 [PMID: 30148991 DOI: 10.1016/j.gie.2018.08.030]
26 **Abu Dayyeh BK**, Acosta A, Camilleri M, Mundi MS, Rajan E, Topazian MD, Gostout CJ. Endoscopic Sleeve Gastroplasty Alters Gastric Physiology and Induces Loss of Body Weight in Obese Individuals. *Clin Gastroenterol Hepatol* 2017; **15**: 37-43.e1 [PMID: 26748219 DOI: 10.1016/j.cgh.2015.12.030]
27 **Hill C**, El Zein M, Agnihotri A, Dunlap M, Chang A, Agrawal A, Barola S, Ngamruengphong S, Chen YI, Kalloo AN, Khashab MA, Kumbhari V. Endoscopic sleeve gastroplasty: the learning curve. *Endosc Int Open* 2017; **5**: E900-E904 [PMID: 28924597 DOI: 10.1055/s-0043-115387]
28 **Saumoy M**, Schneider Y, Zhou XK, Shukla A, Kahaleh M, Aronne L, Sharaiha RZ. A single-operator learning curve analysis for the endoscopic sleeve gastroplasty. *Gastrointest Endosc* 2018; **87**: 442-447 [PMID: 28843586 DOI: 10.1016/j.gie.2017.08.014]
29 **Novikov AA**, Afaneh C, Saumoy M, Parra V, Shukla A, Dakin GF, Pomp A, Dawod E, Shah S, Aronne LJ, Sharaiha RZ. Endoscopic Sleeve Gastroplasty, Laparoscopic Sleeve Gastrectomy, and Laparoscopic Band for Weight Loss: How Do They Compare? *J Gastrointest Surg* 2018; **22**: 267-273 [PMID: 29110192 DOI: 10.1007/s11605-017-3615-7]
30 **Sharaiha RZ**, Kumta NA, Saumoy M, Desai AP, Sarkisian AM, Benevenuto A, Tyberg A, Kumar R, Igel L, Verna EC, Schwartz R, Frissora C, Shukla A, Aronne LJ, Kahaleh M. Endoscopic Sleeve Gastroplasty Significantly Reduces Body Mass Index and Metabolic Complications in Obese Patients. *Clin Gastroenterol Hepatol* 2017; **15**: 504-510 [PMID: 28017845 DOI: 10.1016/j.cgh.2016.12.012]

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