93416_Revision_Auto_Edited.docx

WORD COUNT 2490

TIME SUBMITTED 24-MAY-2024 11:58AM

PAPER ID 109180357

Name of Journal: *World Journal of Gastrointestinal Endoscopy*

Manuscript NO: 93416

Manuscript Type: ORIGINAL ARTICLE

Retrospective Study

Functional Lumen Imaging Probe Use in a High-volume Practice: Practical and Technical Implications

Practical and Technical Implications of EndoFLIP use

Abstract

BACKGROUND

The functional lumen imaging probe (FLIP) is an FDA approved tool to aid the diagnosis and management of esophageal disorders. However, widespread adoption of FLIP remains limited and its utility in high-volume practices remains unclear.

AIM

To analyze large sample data on clinical use of FLIP and provide insight on several technical aspects when performing FLIP.

METHODS

We conducted a retrospective comparative and descriptive analysis of FLIP procedures performed by a single provider at an academic medical center. There was a total of 398 FLIP procedures identified. Patient medical records were reviewed and data regarding demographics and procedural details were collected. Statistical tests, including chi-squared, t-test, and multivariable logistic and linear regression, were performed.

RESULTS

There was an increase in FLIP cases with each successive time period of 13 months (n = 68, 146, 184, respectively) with notable rises specifically for indications of dysphagia and GERD. There was a shift toward use of the longer FLIP balloon catheter for diagnostic purposes (overall 70.4% *vs* 29.6%, $p < 0.01$). Many cases (42.8%) were performed in conjunction with other diagnostics/interventions, such as dilation and wireless pH probe placement. Procedures were nearly equally performed with anesthesia *vs* moderate sedation (51.4% anesthesia), with no major complications. Patients who had anesthesia were less likely to have recurrent antegrade contractions (OR 0.4, 95%CI 0.3-0.8) and were also more likely to have absent contractility (OR 2.4, 95%CI 1.3-4.4).

CONCLUSION

FLIP cases have increased in our practice with expanding indications for its use. Given limited normative data, providers should be aware of several potential technical issues, including the possible impact of sedation choice when assessing esophageal motility patterns.

Key Words: Gastroenterology; Endoscopy; Functional lumen imaging probe; Esophagus; Motility

Core Tip: In this study, we provide both a large sample analysis on FLIP use in our practice and data on several potential technical matters. There has been an increase in FLIP utilization in our practice over time, often paired in conjunction with other diagnostics/interventions such as dilation and/or pH probe placement. Patients who had anesthesia compared to moderate sedation were less likely to have repetitive antegrade contractions and more likely to have absent contractility. Given limited normative data, providers should be aware of these potential issues, including the possible impact of sedation choice when assessing esophageal motility patterns.

INTRODUCTION

The functional lumen imaging probe (FLIP) is an FDA approved tool to aid the diagnosis and management of esophageal disorders by measuring luminal diameter, cross sectional area (CSA), distensibility and motility. The AGA Clinical Practice Committee concluded that FLIP assessment is a "complimentary tool to assess esophagogastric junction (EGJ) opening dynamics and the stiffness of the esophageal wall[1]." ACG clinical guidelines on use of esophageal physiology testing offered similar recommendations for FLIP in diagnosis of esophageal motility disorders[2].

The most useful FLIP metric has been the EGJ distensibility index (EGJ-DI), which is calculated by dividing the CSA at the site of interest by the intra-balloon pressure[3]. The EGJ-DI can be a useful measure of LES relaxation in a variety of scenarios including confirmation of EGJ outflow obstruction[4,5]. In addition, by visualizing esophageal diameter changes along a time continuum, FLIP panometry can assess secondary peristalsis to suggest motility classifications[6-11]. Despite published normative data and expanding publications on its use in a variety of other esophageal disorders such as gastroesophageal reflux disease (GERD) and eosinophilic esophagitis (EoE), practical adoption of FLIP remains limited and information regarding the true utilization of FLIP in high-volume clinical practices are relatively scarce[12-18].

We aim to provide large sample descriptive data on clinical use of FLIP in a high-volume academic practice. In addition, we offer insight on technical aspects of FLIP with regards to two points of variation during FLIP procedures: balloon type used and sedation type. The two available diagnostic balloons, EF-325 (8 cm in length) and EF-322 (16 cm in length), have fundamental differences in that the shorter balloon has less distance between impedance rings, potentially affecting spatial resolution, whereas the longer one provides more data on topography. FLIP is typically performed during endoscopy, either under conscious sedation (mainly midazolam/fentanyl) or monitored anesthesia care (mainly propofol). Given the effects of opiates on esophageal motility, we hypothesized that FLIP parameters may differ, based on the type of sedation used, but again, data to demonstrate this have been scarce[6,19].

MATERIALS AND METHODS

Setting and study population

The study was approved by the Stanford University IRB # 53329. The patient population consisted of patients who had FLIP as part of routine clinical care at Stanford Healthcare. There was a total of 398 FLIP procedures identified between September 2016 through November 2019. If a patient received another FLIP on subsequent occasions, these were counted as separate procedures/data points.

Patients received FLIP for a variety of indications. If multiple indications were listed, then the primary one was determined by the proceduralist upon chart review. If an indication was ambiguous based on symptoms, then chart review would determine which was the primary one. The primary indications were abnormal imaging, abnormal manometry, achalasia, achalasia post therapy, dysphagia, EoE, GERD, and gastroparesis. The indication was listed as "other" if it did not clearly fit into primary categories (e.g., these were amyloidosis, bloating, dissection, diverticulum, scleroderma). If a symptom was listed for indication, then it would be categorized into an appropriate indication if no disease process was also mentioned.

Data collection & Statistical analysis

FLIP was performed during upper endoscopy by a single provider (JOC). Standard FLIP procedures were performed to record diameter, pressure and cross-sectional area at 10mL intervals up to 70mL. Similar procedure protocols have been published previously[3,13,20]. Sedation type for the procedure was at the discretion of the proceduralist and consisted of either conscious sedation (e.g., midazolam and fentanyl) *vs* monitored anesthesia care (e.g., propofol). Subsequently, a retrospective chart review of these procedures was done for analysis. Patient medical records were reviewed and data regarding demographics and procedural details were collected. Statistical tests, including chi-squared, t-test, and multivariable logistic and linear regression, were performed using SAS (Version 9.4. Cary, NC: SAS Institute Inc; 2014).

Measures of interest

For a descriptive measure, FLIP was separated as either diagnostic or therapeutic (EsoFLIP). For diagnostic procedures, all FLIP measurements recorded for analysis purposes were of the gastroesophageal junction (GEJ). For those with indications of gastroparesis, pyloric FLIP was done but measurements and motility patterns were not included in comparative analyses given the different anatomical sites. Additional upper GI procedures done in conjunction with diagnostic FLIP on the same procedure encounter were also recorded, including wireless pH monitoring, non-EsoFLIP dilation and botulinum toxin injection.

For each procedure, the FLIP balloon type used was identified. There are two available diagnostic balloons, EF-325 (8 cm in length, 50mL max volume distention) and EF-322 (16 cm in length, 72mL max volume distention). The catheter used (16 cm *vs* 8 cm) was chosen at the discretion of the proceduralist. FLIP motility patterns, when available, were also collected from procedure reports. These patterns were initially recorded intra-procedure by endoscopist. Patients were classified as having recurrent antegrade contractions, isolated antegrade contractions, retrograde contractions or absent motility.

RESULTS

FLIP trends over time

We identified 398 FLIP procedures over the course of 3 years. The mean age of patients was 55 years and the majority were Caucasian females (Table 1). A third of patients had prior history of foregut surgery and 16.3% were on opioid medications at the time of the procedure. The type of sedation was almost split equally amongst the procedures with 52.5% of the procedures using anesthesia. Among those who received moderate sedation, the median medication doses were midazolam 5 mg and fentanyl 125 mcg. Average procedure time was 21.4 min with anesthesia and 17.0 min with moderate sedation ($p<0.01$).

With each successive time period of 13 months, there was a rise in number of FLIP procedures, with notable rises specifically for indications of dysphagia and GERD (Fig 1a and 1b). This pattern was in conjunction with an increase in outside referrals. There were 22 EsoFLIP dilations done during this time period. Many procedures (42.8%) were performed together with another diagnostic study or intervention, such as dilation, botulinum toxin injection or wireless pH probe placement (Fig 1c). There were no major complications identified.

Impact of sedation type on FLIP

For the 381 esophageal FLIP procedures, the rates of sedation type were similar (51.4% anesthesia *vs* 48.6% moderate sedation; Table 2). Median moderate sedation doses employed were 5 mg midazolam and 125 mcg fentanyl. There were differences in procedure indication between groups (P = 0.01), with more patients with EoE having moderate sedation. More patients on baseline opioids underwent anesthesia (p<0.01). After adjusting for indication and balloon type, procedure time was 4.4 minutes longer, on average, in the anesthesia group (p<0.01). All but one EsoFLIP dilation were done with anesthesia support.

There was a slight statistical difference in diameter measurement at 60cc balloon distention between groups (11.5mm *vs* 12.3mm), but this trend was not seen in any other static measurements or at other distention volumes (Table 3). After adjusting for procedural indication, opioids on medication list and type of balloon, those who had anesthesia were less likely to have recurrent antegrade contractions (OR 0.4, 95%CI 0.3-0.8). They were also more likely to have absent contractility (OR 2.4, 95%CI 1.3-4.4).

Variation based on FLIP catheter

Most diagnostic FLIP procedures (70.4%) were done using the EF-322 balloon (Table 4). There was an increase in EF-322 procedures over time with a decrease in EF-325 procedures (p<0.01). There were differences in procedure indication, with more GERD evaluations performed using EF-322 and more post therapy achalasia and prior foregut surgery evaluations done with EF-325 (49.5% *vs* 26.4%, p<0.01). Procedure sedation type and moderate sedation dosages were similar between the two groups. After adjusting for sedation type, indication, prior foregut surgery and opiate use, balloon type did not affect procedure length (P = 0.49). The variation in FLIP parameters, by balloon type, are shown in Table 5.

DISCUSSION

FLIP has been a key component of our esophageal practice and its use has grown steadily from 2016 through 2019, with increased outside referrals representing more awareness of FLIP in the our community. Indications have changed with time, with earlier studies performed more for patients with achalasia and follow-up of abnormal esophageal manometries, whereas more recently, there has been an increase in use for patients with dysphagia and GERD. Especially with addition of real time panometry, FLIP can theoretically be a more valuable tool for initial evaluation of dysphagia as it can be done at time of endoscopy. Prospective studies are needed to determine if FLIP performed with index endoscopy can have utility in the diagnostic workup of dysphagia.

In our current clinical practice, FLIP is often performed in conjunction with other tests or treatments, with 42.8% percent of FLIP being done in the same endoscopy as wireless pH testing, botulinum toxin injection and/or esophageal dilation in our study. The addition of FLIP does not add much time to endoscopy, as previously demonstrated[20]. Its safety has been excellent, with no major complications. Of the 398 procedures, there were 3 post procedure visits to the emergency department, with complications ruled out at that time.

Given the large sample size of this study's FLIP cohort, we aimed to examine two technical issues which have had limited published data so far. Given the potential impact of endoscopic sedation on esophageal motility, we examined the differences in FLIP parameters based on sedation type. At our institution, this is most commonly propofol when anesthesia is utilized *vs* midazolam/fentanyl when conscious sedation is used. After adjusting for procedure indication, patient opioid use, and type of balloon used in our regression algorithm, sedation type did not seem to have a meaningful impact on measurements of distensibility or diameter. However, interestingly, even when these factors were adjusted, we noted that those who underwent anesthesia compared to moderate sedation were less likely to exhibit normal motility patterns on FLIP. Though not looking directly at the same issue, this is seemingly in contrast to the study by Carlson et. al in which 21% of cases performed with monitored anesthesia care in which differences between patterns of esophageal manometry peristalsis and FLIP panometry were not observed related to sedation type[6]. Though we did try to statistically control for some confounders in our data, it is possible that the increase in abnormal motility in patients undergoing anesthesia represents a selection bias wherein patients with increased disease burden were selectively referred for anesthesia over conscious sedation. However, there is no evidence from our data that dysmotility was more likely be seen in patients receiving periprocedural opiates (in the form of conscious sedation), which was our initial concern leading to this analysis.

We also found that EF-322 use has increased over time. Though there is some selection bias, this is likely reflective of increasing adoption of esophageal peristalsis measurements. The EF-325 catheter was still used limitedly for some indications such as symptoms after achalasia therapy and follow-up from prior abnormal studies incorporating the shorter balloon. The EF-325 catheter was also used exclusively for pyloric evaluation; however, that data was not included in this analysis. Not unexpectedly, both balloons demonstrated increasing diameter and distensibility with increasing balloon volume. Given limited normative data with FLIP, these findings may have important clinical implications and demonstrates the importance of well-defined protocols, as terminating a study with the EF-322 catheter at 60mL of balloon distention may lead to different interpretations than if a study were to be completed to 70mL.

Though our study includes both descriptive and comparative analyses of practical and technical aspects of FLIP in a large cohort, there are still several limitations. First, this is a retrospective study and is subject to selection bias as discussed previously. Though having a single provider performing FLIP procedures reduces variability and increases internal validity, the patterns of FLIP use we present may vary from other high-volume practices. We also do not have manometric data available to correlate with our FLIP panometry patterns. Though we do control for certain potential confounders in our regression model, having correlation with manometry findings would strengthen our findings of altered contractile patterns based on sedation type. Regardless, we do feel this is a potentially important finding and warrants further evaluation.

CONCLUSION

In conclusion, FLIP use has increased over the past several years with evaluation of dysphagia becoming increasingly more common among other expanding indications. Given limited normative data, providers should be aware of several potential technical issues, including the possible impact of sedation choice when assessing esophageal motility patterns on FLIP. As this technology gains more awareness in the community, more outcome-based studies will be needed to evaluate both its utility in early evaluation of dysphagia as well as expanding indications for its use.

93416_Revision_Auto_Edited.docx

ORIGINALITY REPORT

2%
SIMILARITY INDEX

PRIMARY SOURCES

1	www.ncbi.nlm.nih.gov Internet	30 words — 1%
2	"Abstracts from the 2022 American Foregut Society Annual Meeting", Foregut: The Journal of the American Foregut Society, 2022 Crossref	16 words — 1%
3	Ikuo Hirano, John E. Pandolfino, Guy E. Boeckxstaens. "Functional Lumen Imaging Probe for the Management of Esophageal Disorders: Expert Review From the Clinical Practice Updates Committee of the AGA Institute", Clinical Gastroenterology and Hepatology, 2017 Crossref	12 words — < 1%

EXCLUDE QUOTES	ON	EXCLUDE SOURCES	< 12 WORDS
EXCLUDE BIBLIOGRAPHY	ON	EXCLUDE MATCHES	< 12 WORDS