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Comparison between an angled-tip and straight-tip guidewire in biliary cannulation: a prospective, randomized trial

Principle Investigator:

Ann Marie Joyce MD

Program Director, Advanced Endoscopy Fellowship

Director of Advanced Endoscopy

Clinical Associate Professor of Medicine, Tufts University School of Medicine

Division of Gastroenterology and Hepatology

Lahey Hospital and Medical Center

Sub-Investigators:

Samson Ferm MD

Advanced Endoscopy Fellow

Division of Gastroenterology and Hepatology

Lahey Hospital and Medical Center

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Research Objectives/Specific Aims/Outcomes Measures

Wire-guided cannulation of the common bile duct is a standard technique utilized during Endoscopic Retrograde Cholangio-Pancreatography (ERCP) to ensure safe and effective access to the common bile duct via the ampulla of Vater. Due to the anatomy of the ampulla, and the orientation of the biliary orifice, a guidewire with an angled tip may allow easier and safer access to the common bile duct without inadvertent manipulation of the pancreatic duct. We aim to assess the technical and clinical outcomes between an angled-tip guidewire (GW) compared to a straight-tip guidewire in wire-guided cannulation of the common bile duct. We hypothesize that an angled-tip GW is associated with increased rate of successful cannulation, decreased procedure time and decreased rate of post-ERCP pancreatitis in wire-guided biliary cannulation during ERCP.

Primary Research Question:

Is the use of an angled-tip guidewire associated with increased rate of successful cannulation of the common bile duct in ERCP?

Secondary Research Questions:

Is the use of an angled-tip guidewire associated with decreased procedure duration?

Is the use of an angled-tip guidewire associated with reduced rates of post-ERCP pancreatitis?

Is cannulation more successful using an angled-tip wire in a particular type of papilla?

Background Information / Significance / Scientific Rationale

Endoscopic Retrograde Cholangio-pancreatography is a commonly performed procedure for diagnostic and therapeutic purposes in the setting of biliary tract pathology. During ERCP, bile duct access is performed with use of a catheter (sphincterotome) that is passed beyond the papilla into the bile duct. The utilization of a guidewire, over which the catheter is passed, to ensure selective common bile duct cannulation (as opposed to pancreatic duct cannulation) is associated with improved overall cannulation rates and lower risks of post-ERCP pancreatitis, and this practice has become standard.[1] A variety of guidewires are available to the endoscopist. The guidewires vary in size, stiffness and design of the tip of the wire, which may be straight, angled, J-shaped or tapered. Angled-tip guidewires were shown to result in decreased procedure duration, with a similar rate of cannulation and complications as compared to a straight tipped wire in a randomized-controlled trial including 239 patients.[2] Aside from this RCT, there is a paucity of literature that compares angled-tip and straight tip-guidewires in

biliary cannulation. In theory, an angled-tip guidewire may result in better technical performance including rate of successful cannulation, duration of procedure, and incidence of post-ERCP pancreatitis because of the anatomy of the ampulla of Vater and the oblique trajectory of the biliary orifice. Our goal is to compare the rate of successful cannulation, duration of procedure and incidence of post-ERCP pancreatitis between an angled-tip guidewire and straight-tip guidewire. This study will aid in the performance of ERCP and in the proper selection of devices to ensure safe and effective biliary cannulation. Additionally, this research may reduce healthcare expenditure by identifying an alternative device that may reduce the duration of the ERCP procedure.

Participant Selection / Eligibility

Patients undergoing ERCP with native papilla and pancreatico-biliary disease who are candidates for ERCP with biliary cannulation are eligible for enrollment. Subjects must meet all inclusion criteria in order to be eligible to participate in the study.

Inclusion Criteria:

Patients undergoing ERCP for cholangiography, bile or tissue sampling from the gallbladder or bile duct, or for treatment of biliary diseases (removal of common bile duct stones, biliary stent placement)

Exclusion Criteria:
Patients who are less than 18 years old
Pregnant patients
Patients who have undergone previous bile duct cannulation or sphincterotomy
Patients who have undergone prior endoscopic balloon dilation or needle-knife fistulotomy
Patients who have undergone gastric surgery (Billroth gastrectomy II, Roux-en-Y gastric bypass)
Patients with acute pancreatitis
Patients who refuse endoscopic intervention
Patients with ampullary tumor, duodenal stenosis, or pre-operatively proven pancreaticobiliary malunion

Subjects will be recruited based upon their need to undergo ERCP for biliary diagnosis or therapy as determined by the principal investigator or sub-investigators. This determination will be made based upon the clinical requirement of endoscopic biliary cannulation. Subjects will be either inpatients or outpatients who require ERCP and bile duct cannulation. The overall sample size will be approximately 248 patients. Pregnant women will not be recruited for participation in this study as ERCP in certain pregnancies may be harmful to the fetus especially during the first trimester. Additionally, minors (age less than 18 years old) and prisoners will not be recruited or enrolled in the study, as these are vulnerable populations who may have a compromised ability to make an informed decision about participation.

Subject Enrollment

All patients enrolled in the study will be required to sign an informed consent form to participate in the study as well as for the resultant data to be collected and used for analysis and eventual publication. Consent will be obtained via a paper consent form on the day of procedure by the research team. A copy of the consent form will be made and given to the subject and the original copy will be stored in a secure file on site. All known risks, benefits and alternative therapies will be explained to the patient by either the PI or sub-investigators prior to signing the consent form. The patient will be randomized to a study arm in a 1:1 fashion by a computer-generated random number list via the REDCap Electronic Data capture application after informed consent has been obtained and just prior to the start of the procedure by either the PI or the sub-investigators.

Study Design and Procedures

This is a prospective, randomized, unblinded trial performed at Lahey Hospital and Medical Center. All procedures will be performed by experienced advanced endoscopists with over 2000 career ERCP's and 350 ERCP's performed per year, (or by the advanced endoscopy fellow under supervision of the attending gastroenterologist). Enrolled patients will be randomly assigned by a computer-generated number list to 2 groups (group 1, angled-tip GW; group 2, straight-tip GW). All procedures will be performed using standard duodenoscope or Exalt duodenoscope (JF-260V; Olympus Medical Systems Corp, Tokyo, Japan). For the procedure, patients will receive either general anesthesia or monitored anesthesia care as clinically indicated. Medications will be administered by a licensed anesthesiologist or CRNA. All procedures will be performed via short-wire technique using a 0.025-inch, 260cm-long angled guidewire with 5-cm hydrophilic tip (Jagwire Revolution, Boston Scientific, Natick, MA) or a 0.025-inch, 260-cm long straight guidewire with a 5-cm hydrophilic tip. (Jagwire, Boston Scientific, Natick, MA) For cannulation, attending gastroenterologists will be allowed 5 minutes to cannulate (from first contact of ampulla) or 5 passes inadvertently into the pancreatic duct (whichever occurs first). If the procedure is performed by gastroenterology fellow, the fellow will be allowed 5 minutes from first contact with the ampulla or 5 passes into the pancreatic duct (whichever occurs first). If the pancreatic duct is cannulated, double guide-wire technique will be performed with the same wire (0.025-inch guidewire) for an additional 5 minutes. If cannulation remains unsuccessful, needle-knife technique will be performed with pancreatic duct stenting performed. This protocol is similar to Vihervaara et al.[2] Post-procedurally, patients will be monitored for post-ERCP pancreatitis with either inpatient follow-up or via a phone call if procedure performed as outpatient. Post-ERCP pancreatitis will be defined as new or worsened abdominal pain combined with >3 times the normal value of lipase more than 24 hours after ERCP and requirement of hospital admission or prolongation of a planned admission. Routine blood work will be collected upon admission and during hospitalization as clinically warranted. Data will be collected using the REDCap data collection application and will be securely stored on LHMC secured servers.

Standard of Care: Procedure in both treatment groups is considered standard of care as they use FDA approved devices. Here at Lahey, The endoscopists use both guidewires. The guidewire is selected based on physician preference. While they typically start with a straight-tip wire, they would also use angled-tip guidewire if the straight tip guidewire does not achieve cannulation of the bile duct. Data shows that both guidewires are safe to use with similar rates of successful cannulation and adverse events.

Study Calendar / Schematic / Schedule

The main study-required visit will be the day of the planned procedure (ERCP). On this visit, the pre-procedural process will include a discussion with the patient regarding the risks and benefits of the procedure as well as a description of the study and consent for participation in the study. Pre-procedure data will be collected and entered into the data capture tool. The data collected will include patient demographics and indication for procedure. Randomization will then be performed immediately prior to the start of the planned procedure and the randomization assignment will be entered into the data capture tool. Data will then be collected immediately after the procedure and will include procedure duration, successful cannulation determination, pancreatic duct cannulation determination, types of guidewires used during procedure, fellows involvement in procedure and complications of procedure. On post-procedure day one to post procedure day five, post-procedural data will be collected by either inpatient assessment or by a telephone call to the subject if the procedure was performed on an outpatient basis by either the PI or sub-investigators. If there is a concern for possible post-ERCP pancreatitis, a lipase level will be checked on an inpatient or outpatient basis. There will be no other planned study-required visits after post-procedure day five. Subjects will be removed from enrollment if they choose to withdraw from the study.

Potential Risks and Discomforts

The main risk of participation in this study is breach of confidentiality that pertains to data collection. This risk will be addressed in the “data management” section. There will be no additional risk to subjects based upon randomization to either arm of the study as data has shown that either wire (angled-tip vs straight-tip) are equally safe and confer no higher risk of adverse events.[2]

The risk associated with ERCP includes bleeding, infection, perforation or post-ERCP pancreatitis.[3] The risk of bleeding is 1.3%.[3] The risk of infection (ascending cholangitis) is less than 1%.[3] The risk of perforation is 0.1 to 0.6%.[3] The risk of post-ERCP pancreatitis is 3.5%.[3] These risks can range from mild in severity to severe and life threatening. These risks will be minimized by virtue of the procedures being performed by or under the supervision of experienced endoscopists with over 2000 procedures performed and by following evidence-

based practice in the pre, intra, and post-procedural care of the subjects. Adverse events will be reported to the appropriate Lahey Hospital and Medical Center committee and to the IRB.

Potential Benefits

Aside from the benefit from the procedure itself for therapeutic and diagnostic purposes, patients will not directly benefit from the research being performed. We hope that our findings will have benefits for future patients undergoing the ERCP procedure.

Statistical Analysis

The sample size needed to achieve statistical significance for the primary outcome is 248 (207 *1.2) after adding 20% screen failure rate. The power of the study to detect if there is a true difference will be 0.80. It will take approximately six months to reach the target accrual**.** The variables that need to be collected include demographics, co-morbidities, laboratory values, date of procedure, diagnosis, outcome of procedure (success of cannulation), duration of procedure, post-procedure complications (including post-ERCP pancreatitis) and fellow involvement in procedure. The outcome variables include rate of successful cannulation, and incidence of post-ERCP pancreatitis. Predictor variables include co-morbidities, indication for procedure and fellow involvement in procedure. Potential confounding variables include differing anatomy of papilla amongst subjects, underlying etiology of biliary obstruction (which may be different from suspected pre-procedure diagnosis) or unforeseen biliary pathology which alters procedure. The study endpoints will be achieved by showing a statistically significant difference in the rate of successful cannulation using an angled-wire as compared to a straight wire as defined as a p-value of less than 0.05. The proportion of procedures that are successful in the two treatment arms will be compared using chi squared analysis. Similarly, the rate of development of pancreatitis will be compared using chi squared analysis. The total duration of the procedure will be compared using a T-Test for comparing mean if the data are normally distributed or a Wilcoxon rank sum test if not normally distributed.

Data Management

All data will be collected using the REDCap Data Collection application and will be stored electronically on this platform. Only the PI and sub-investigators will have access to the password encrypted REDCap database. There will be no transmission of the acquired data off site. The data set will not include patient names or other identifiers. Information for this study will be available as required to the FDA, Massachusetts Department of Health, and LHMC IRB. Names of subjects will not be mentioned in publications or case reports.

Data and Safety Monitoring and Quality Assurance

The principal investigator will be responsible for data and safety monitoring and quality assurance. This will be conducted by weekly team meetings to review the consent process; collection of data and post-procedural follow up of study subjects. Additionally, there will be a bi-weekly review of the accuracy and completeness of the database and of the storing of completed consent forms in the appropriate secured file on the LHMC campus. The sub-investigators will report directly to the PI any possible breach in protocol and will be responsible for regularly monitoring for quality assurance of the study protocol.

References:

[1] Cennamo V, Fuccio L, Zagari RM, Eusebi LH, Ceroni L, Laterza L, Fabbri C, Bazzoli F. Can a wire-guided cannulation technique increase bile duct cannulation rate and prevent post-ERCP pancreatitis?: A meta-analysis of randomized controlled trials. Am J Gastroenterol. 2009;104:2343–2350.

2 Vihervaara H, Grönroos JM, Koivisto M, Gullichsen R, Salminen P. Angled- or straight-tipped hydrophilic guidewire in biliary cannulation: a prospective, randomized, controlled trial. Surg Endosc. 2013 Apr;27(4):1281-6. doi: 10.1007/s00464-012-2596-6. Epub 2012 Dec 19. PMID: 23250671.

3 ASGE Standards of Practice Committee, Anderson MA, Fisher L, Jain R, Evans JA, Appalaneni V, Ben-Menachem T, Cash BD, Decker GA, Early DS, Fanelli RD, Fisher DA, Fukami N, Hwang JH, Ikenberry SO, Jue TL, Khan KM, Krinsky ML, Malpas PM, Maple JT, Sharaf RN, Shergill AK, Dominitz JA. Complications of ERCP. Gastrointest Endosc. 2012 Mar;75(3):467-73. doi: 10.1016/j.gie.2011.07.010. PMID: 22341094.