A pilot randomized trial to study the success rate of early precut fistulotomy and its effect on radiation dose in patients with difficult biliary cannulation

H.S. Mandavdhare[1], J. Shah[1], R. Kakadiya[1], P. Kumar M.[2], P. Gupta[3], H. Singh[4], V. Sharma[1], U. Dutta[1]

(1) Department of Gastroenterology, (2) Department of Pharmacology, (3) Department of Radiodiagnosis, (4) Department of Surgery, Post Graduate Institute of Medical Education and Research, Chandigarh, India.

Abstract

Background: **Role of precut fistulotomy in reducing fluoroscopy time and the radiation dose in difficult selective biliary cannulation is unknown.**

Methods: **We performed a randomized trial where patients with difficult biliary cannulation were randomized into 2 groups: early precut fistulotomy (precut five minutes after failed standard biliary cannulation) or late precut fistulotomy (precut fifteen minutes after failed standard biliary cannulation). We compared the success rates of selective biliary cannulation, fluoroscopy time, radiation dose, complication rates, need for repeat endoscopic retrograde cholangiography (ERC) and need for other interventions**

Results: **Of the 130 eligible patients screened, 40 patients were randomized. The technical success was comparable between early and late group. The fluoroscopy time and radiation dose were significantly less in the early group [4 minutes (3, 6) vs 15 minutes (8, 28), p=0.001] and [1.35 mGy (0.90, 1.63) vs 2.40 mGy (1.58, 3.25), p=0.010] respectively. In the late group, 60% required need for rescue precut fistulotomy. One patient from late group developed post ERC pancreatitis while 1 from early group developed perforation. Three needed other interventions due to failed second attempt.**

Conclusion: **Early precut fistulotomy has comparable technical success and reduces the radiation dose as compared to late precut fistulotomy for difficult biliary cannulation.** (Acta gastroenterol. belg., **2021,** 84**, 557-561**).

Keywords: Precut, fistulotomy, success, fluoroscopy, radiation dose.

Introduction

Selective biliary cannulation is the prerequisite for successful biliary interventions in endoscopic retrograde cholangiography (ERC). Even experienced endoscopists may encounter difficulty in a third of patients including failure to cannulate or inadvertent pancreatic duct cannulation (1). In these patients various precut techniques may be required to access the bile duct like precut papillotomy and precut fistulotomy. Some studies have demonstrated the safety of precut fistulotomy with adverse events comparable to the standard cannulation technique (2-4). However, it is unclear if early institution of precut fistulotomy could reduce the fluoroscopy time and hence the radiation exposure. It should be our endeavor to minimize the radiation dose to as low as possible as per the ALARA (As Low As Reasonably Achievable) principle (5). The European society for gastrointestinal endoscopy (ESGE) has advised to record patient radiation dose in national database in order to formulate reference levels, so that patients get minimum exposure when such reference levels are adhered to (6). We report findings from this randomized trial to compare between early and late precut fistulotomy designed to address the issue of safety of early fistulotomy and its impact on reducing the fluoroscopy time and radiation exposure.

Methods

This was a prospective randomized trial conducted at a tertiary care center in North India from April 2019 till February 2020. We followed the Consolidated Standards of Reporting Trials guidelines for this study. The study was prospectively registered in ctri.nic.in (CTRI/2019/04/018618) after taking approval from Institute Ethics Committee (NK/4997/Study/164). The study protocol conforms to the ethical guidelines of the Declaration of Helsinki. All patients with naïve papilla posted for ERC and willing to give written informed consent for the study were screened. We included patients with failure to achieve selective biliary cannulation within 5 minutes as per standard definition (7). Those with an altered anatomy- Billroth II, periampullary diverticulum, coagulopathy- International normalised ratio>1.5, low platelet count< 1 lac/mm^3, suspected periampullary growth and very small/flat papilla were excluded. The primary objective of the study was to compare the success rate of selective biliary cannulation. Other outcome parameters which were compared between the two groups included 1) fluoroscopy time and dose, 2) complication rate, 3) need for repeat ERC and 4) need for other interventions. All patients underwent routine investigations for diagnosis of biliary obstruction before ERC. As per our institutional protocol, every patient received rectal indomethacin suppository 100mg before the procedure and intravenous fluid resuscitation peri-procedure. Group I included patients randomized to early precut fistulotomy which was performed immediately after five minutes of attempted biliary cannulation and Group II included those who were randomized to late

Correspondence to : Harshal S Mandavdhare, Assistant Professor, Department of Gastroenterology, Postgraduate Institute of Medical Education and Research, F block, Nehru Hospital, PGIMER, Chandigarh, India-160012. Phone: +91959281487.
E-mail : hmandavdhare760@gmail.com

Submission date : 17/10/2020
Acceptance date : 15/03/2021

precut fistulotomy where the precut was performed after 15 minutes of failed biliary cannulation.

Standard cannulation and fistulotomy techniques

The endoscopist who performed the fistulotomy had experience of performing >300 ERCPs per year of which 10-15% are fistulotomy, which the endoscopist has been doing for last 2 years. The ERC was performed under conscious sedation and EVIS EXERA II video duodenoscope was used for all the procedures (TJFQ180V, Olympus, Tokyo, Japan).

Standard cannulation

This was done in the usual fashion with the help of triple lumen sphincterotome (Ultratome XL, Boston Scientific, USA) that was preloaded with guidewire. Once the tip of the sphincterotome got engaged through the papillary orifice into the ductal bay, the wire was advanced under fluoroscopic guidance and selective biliary cannulation was confirmed with the help of water soluble contrast cholangiogram. During the standard cannulation attempt, if it was not possible to cannulate with the sphincterotome, we would switch over to other catheters as per our discretion.

Fistulotomy (Figure 1)

Fistulotomy was performed with needle knife fistulotome (Microknife™ XL, Boston Scientific, USA) according to standard technique(8,9). The basic steps of fistulotomy were 1) a linear incision made 2-3 mm above and separate from the papillary orifice with the help of Microknife XL (ENDOcut I mode-effect 2, watt-60, ERBE, Tubingen, Germany) in a below upward direction, 2) deepening the incision in a step wise manner till the whitish muscle layer of the sphincter is visualised, 3)cutting the muscle layer leading to a gush of bile and 4) wire guided cannulation deep into the biliary system confirmed by cholangiography.

Fluoroscopy and adverse events

We recorded the fluoroscopy time in minutes and dose in milli-Gray, as were the number of inadvertent PD cannulations in each group. All fluoroscopy procedures were done using pulsed fluoroscopy on a digital fluoroscopy system with flat-panel detectors (Artis Zee, Siemens, Erlangen, Germany) using a frame rate of 7.5 frames per seconds. Technical success was defined by successful selective biliary cannulation. ERC time (total procedure time) was calculated from first contact of sphincterotome with the papilla for cannulation attempt to successful selective biliary cannulation. Fluoroscopy time was calculated as total duration of fluoroscopy required to guide the biliary cannulation from first attempt to successful biliary cannulation in minutes.

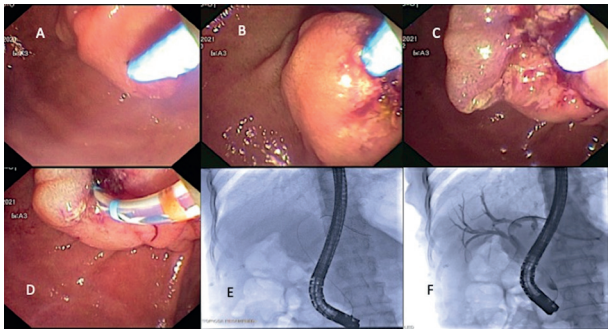

Figure 1. — A- Tip of needle knife positioned at the site where incision is to be taken. B- Incision done and cut deepened. C- Cut extended to split the ampullary tissue and expose the muscle of lower end of common bile duct. D- Cannulation attempt after incising the muscle. E- Fluroscopic view showing the guidewire going into the left biliary system. F- Cholangiogram confirms selective deep biliary cannulation.

Adverse events were recorded by an independent person not involved in the procedure according to standard guideline(10). After the procedure, patients were observed for 6 hours and admitted if they developed abdominal pain, guarding and vomiting consistent with post ERC pancreatitis (PEP). The amylase and lipase levels were done 24 hours post procedure to confirm the PEP.

Randomization and Statistical analysis

Randomization was done by computer-generated random number sequence by an independent person not related to the study. Allocation was concealed using serially numbered opaque sealed envelope technique. As this was a pilot trial, a formal sample size calculation was not done and we arbitrarily recruited 40 patients (20 in each group). The randomization and allocation process was done by an independent person who was not involved in the intervention. At 5 minutes of failed biliary cannulation, an assistant would open the envelope and reveal the number. The statistical analysis was performed using R statistical software version 3.6.1. For comparison between two groups, independent t test was used for parametric data and Mann Whitney U test was used for non-parametric data. The categorical data were represented as number along with column percentages and compared either with chi-square test of independence (if all values >5) or Fisher exact test. P value <0.05 was taken as statistically significant.

Results

From April 2019 to February 2020, 130 patients with naive papilla were screened of which 90 patients were excluded (technical success in 5 minutes-49, periampullary diverticulum-13, coagulopathy/thrombocytopenia-11, small flat papilla-9, periampullary growth-7 and altered anatomy-1) (Figure 2). Eventually, 40 patients were

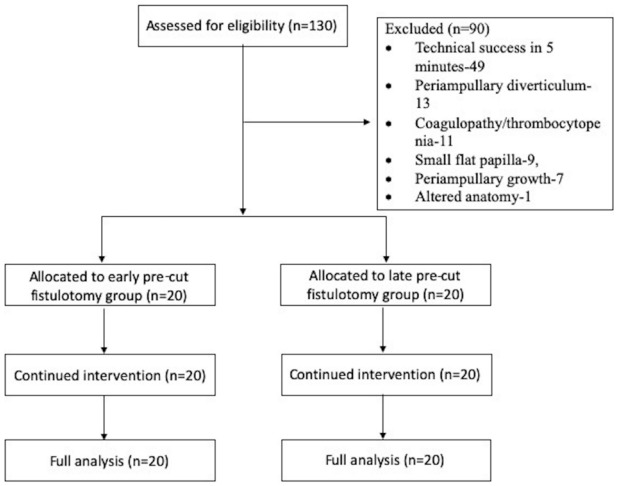

Figure 2. — Consort flowchart for the study.

randomized into the early and late group (20 each). Both groups were similar in age, gender and indications for ERC (Table 1). Overall technical success was equal in both the groups (90% vs 95%; p>0.9). However, in late pre-cut fistulotomy group, 12 (60%) patients still required pre-cut fistulotomy for biliary cannulation. The ERC time was less in early group compared to late group [12 minutes (8, 17) vs 18 minutes (12, 23); p=0.085]. Similarly, fluoroscopy time (FT) and radiation dose were also significantly less in early group {1.35 (0.90, 1.63) vs 2.40 (1.58, 3.25), p=0.01} and dose in mGy {4 (3, 6) vs 15 (8, 28), p=0.001, respectively}. Three patients (two patients from early group and one from late group) had failed biliary cannulation even on the second attempt. One patient from early group underwent successful endoscopic ultrasound guided rendezvous procedure as a rescue measure while rest two patients (one patient from each group) underwent percutaneous transhepatic biliary drainage as rescue. One patient from the early group developed perforation (type II) that required surgical drainage of a retroperitoneal collection and recovered. One patient from the late group developed moderate PEP and recovered with conservative management (Table 2).

Table 1. — **Showing baseline characteristics of the study subjects**

Characteristic[1]	Early (N = 20)	Late (N = 20)	*p*-value[2]
Age	48 ± 18	53 ± 17	0.4
Male	11 (55%)	6 (30%)	0.2
Indication			
Benign stricture	2 (10%)	1 (5.0%)	0.4
Choledocholithiasis	13 (65%)	13 (65%)	
Malignant stricture	3 (15%)	6 (30%)	
Others[U]	2 (10%)	0 (0%)	

U- Common bile duct injury with bile leak and Gall bladder perforation.

Discussion

Our study showed similar final success rates among both the groups (90% vs 95%) which is in line with a previous study. Lopes L et al. had compared early versus late precut fistulotomy and showed final biliary cannulation success after fistulotomy among both the groups was similar (93% vs 83%) (8). In the conventional method, 60% of the patients required rescue (late) precut fistulotomy for biliary cannulation which signifies the limited usefulness of continuing the conventional biliary cannulation attempt in patients with difficult biliary cannulation. These findings corroborate with previous retrospective studies comparing pre-cut fistulotomy vs conventional methods of biliary cannulation (11,12).

While the earlier belief was that precut fistulotomy was associated with increased risk of PEP, however, it is now understood that the papillary manipulation for a long time before attempting precut fistulotomy technique is responsible for increased rate of PEP (11-13). As precut fistulotomy avoids papillary manipulation, theoretically, it should be associated with reduced risk of PEP (4). A recent multicenter randomized trial has shown the high safety of precut fistulotomy as a primary method of biliary cannulation in high risk PEP cohort. The success rate was significantly higher (98% vs 90%, p=0.005) and none of the patients in the precut group developed PEP (0 vs 9.2%, p=0.001), while other adverse events were comparable. Although, the mean cannulation time was

Table 2. — **Showing results of the study**

Characteristic[1]	Early (N = 20)	Late (N = 20)	*p*-value[2]
>1 PD guide wire passage and PD stenting done	5 (25%)	5 (25%)	>0.9
Failed first attempt	3 (15%)	1 (5.0%)	0.6
Need for rescue fistulotomy	NA	12 (60%)	-
Over all Technical Success	18 (90%)	19 (95%)	>0.9
Total ERC time (min)	12 (8, 17)	18 (12, 23)	0.085
Total fluoroscopy time (min)	1.35 (0.90, 1.63)	2.40(1.58, 3.25)	0.010
Radiation exposure (mGy)	4 (3, 6)	15 (8, 28)	0.001
Adverse Events			
Post ERC pancreatitis	0	1	
Perforation	1	0	

longer in the precut group, this was due to the stringent failure criteria of the conventional group in which participants with longer time may have been excluded from the time calculation (4).

In our study, early needle knife fistulotomy was associated with lesser cannulation time while the fluoroscopy requirement, both time in minutes {1.35 (0.90, 1.63 vs 2.40 (1.58, 3.25), p=0.01} and dose in mGy {4 (3, 6) vs 15 (8, 28), p=0.001}, was significantly less in the early group. None of the previous studies have explored the role of early pre-cut fistulotomy in reducing fluoroscopy requirement. There are various measures that can be advocated to reduce the radiation dose to the patient during ERCP to achieve ALARA. These are 1) placing the patient as far as possible from the X ray tube, 2) keeping the FT as low as possible, 3) using lowest pulse rate of fluoroscopy, 4) using lowest acceptable image quality during fluoroscopy, 5) collimating the beam to the smallest acceptable size, 6) avoiding needless magnification, 7) using the last spot image, 8) increasing the tube voltage that allows acceptable image quality and 9) complex procedure to be performed by experienced endoscopist to reduce the FT(6). Among these the simplest measure is to reduce the FT. The effects of radiation are of 2 types 1) dose related tissue reactions which are immediate (e.g-skin burns, hair loss) and 2) dose independent stochastic effects (cancer risk and genetic defects) which are delayed (6). Hence, to reduce the risk of above 2 effects it would be reasonable to reduce the FT. A recent large retrospective study has shown difficult biliary cannulation (> 5 minutes) increases dose area product (DAP) and FT (14). Some guidelines recommend patient dose recording only when the entrance skin dose (ESD) measures 1-2 Gy for a procedure. As per the USFDA, ERCP doesn't have such an amount of exposure (mean ESD of 55-347 mGy) (6). However, a recent large cohort study has shown that even low dose radiation exposure is potentially carcinogenic (15). Hayashi S et al have demonstrated that endoscopist experience can reduce the dose in difficult procedures (proximal malignant biliary obstruction), however, still it is significantly more compared to easy procedures (distal malignant obstruction and CBD stones) (16). In patients with difficulty in cannulation, early application of precut fistulotomy would reduce the FT and thus radiation dose to some extent. In the present study, the early fistulotomy group had significantly less FT and dose compared to late group for difficult selective biliary cannulation. This could become even more important in difficult procedures where an early application of precut fistulotomy could reduce the radiation dose for the particular procedure.

In our study, 1 patient from the late group developed moderate PEP which required hospitalization for 1 week and was successfully managed conservatively while none of the patients from early group developed PEP. One patient from the early group developed perforation which required surgical drainage of a retroperitoneal collection. ESGE guidelines suggest that wherever possible if the perforation is amenable for endoscopic closure, it should be attempted to avoid surgery (17). In our case, the perforation was not obvious during ERCP and the patient developed severe pain abdomen and vomiting during the post ERCP observation eventually developing retroperitoneal collection that was drained and patient improved subsequently.

One fourth of patients from both the groups had inadvertent pancreatic duct cannulation. In such scenario, trans-pancreatic sphincterotomy is an alternative option for SBC in difficult cannulation. In a recent systematic review and meta-analysis, trans-pancreatic sphincterotomy has shown superior selective biliary cannulation success compared to double guide wire and precut papillotomy, while, it was comparable to precut fistulotomy. The PEP rate was comparable between trans-pancreatic sphincterotomy and double guide wire/ precut papillotomy while it was more with trans-pancreatic sphincterotomy when compared with precut fistulotomy. Rest of the other adverse events were comparable between trans-pancreatic sphincterotomy and other techniques (18).

There are certain limitations to our study. As it was a pilot trial so the sample size was small and the study was done at a single center. Multicentric, larger, prospective trials are required to explore the role of early pre-cut fistulotomy in reducing the radiation dose in difficult biliary cannulation and hence reducing the total dose at the end of the procedure. To continue this preliminary endeavor, we have also planned a larger randomized trial with the primary objective to study the effect of precut fistulotomy (early versus late) on fluoroscopy time and radiation dose in patients with difficult biliary cannulation. Also use of rectal indomethacin suppository could be a confounding factor for PEP rate due to fistulotomy per se but this demonstrates that it doesn't completely reduce the risk as the 1 patient had developed PEP in the late fistulotomy group. It has been shown that rectally administered NSAIDS reduce PEP but the risk does not disappear completely. Although it would be prudent to use the lowest frame rate to decrease the radiation dose, however, this may compromise image quality. There is as yet no objective scale that defines the lowest limit of frame rate with acceptable image quality.

Conclusion

Our randomized trial suggests that early pre-cut fistulotomy is associated with similar technical success and lesser cannulation time and fluoroscopy requirement compared to late pre-cut fistulotomy in patients with difficult biliary cannulation.

Conflict of interest

None.

Funding

None.

Trial registration number

CTRI/2019/04/018618

References

1. TESTONI PA., TESTONI S., GIUSSANI A. Difficult biliary cannulation during ERCP: how to facilitate biliary access and minimize the risk of post-ERCP pancreatitis. *Dig Liver Dis.*, 2011,**43**: 596-603.
2. JIN YJ., JEONG S., LEE DH. Utility of needle-knife fistulotomy as an initial method of biliary cannulation to prevent post-ERCP pancreatitis in a highly selected at-risk group: a single-arm prospective feasibility study. *Gastrointest Endosc*., 2016;**84**: 808-813.
3. LIM JU., JOO KR., CHA JM., SHIN HP., LEE JI., PARK JJ., *et al*. Early use of needle-knife fistulotomy is safe in situations where difficult biliary cannulation is expected. *Dig Dis Sci.*, 2012, **57**: 1384-90.
4. JANG SI., KIM DU., CHO JH., JEONG S., PARK J-S., LEE DH., *et al*. Primary Needle-Knife Fistulotomy Versus Conventional Cannulation Method in a High-Risk Cohort of Post-Endoscopic Retrograde Cholangiopancreatography Pancreatitis. *Am J Gastroenterol*., 2020;**115**: 616-624.
5. CAMPBELL N., SPARROW K., FORTIER M., PONICH T. Practical radiation safety and protection for the endoscopist during ERCP. *Gastrointest Endosc*., 2002, **55**: 552-7.
6. DUMONCEAU J-M., GARCIA-FERNANDEZ FJ., VERDUN FR., CARINOU E., DONADILLE L., DAMILAKIS J., *et al*. Radiation protection in digestive endoscopy: European Society of Digestive Endoscopy (ESGE) guideline. *Endoscopy*., 2012, **44**: 408-21.
7. TESTONI PA., MARIANI A., AABAKKEN L., ARVANITAKIS M., BORIES E., COSTAMAGNA G., *et al.* Papillary cannulation and sphincterotomy techniques at ERCP: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. *Endoscopy*., 2016, **48**: 657-83.
8. LOPES L., DINIS-RIBEIRO M., ROLANDA C. Early precut fistulotomy for biliary access: time to change the paradigm of "the later, the better"? *Gastrointest Endosc.*, 2014, **80**: 634-641.
9. ARCHIBUGI L., MARIANI A., CAPURSO G., TRAINI M., PETRONE MC., ROSSI G., *et al*. Needle-knife fistulotomy vs. standard biliary sphincterotomy for choledocholithiasis: common bile duct stone recurrence and complication rate. *Endosc Int Open.*, 2019, **7:**:E1733-E1741.
10. ASGE Standards of Practice Committee, CHANDRASEKHARA V., KHASHAB MA., MUTHUSAMY VR., ACOSTA RD., AGRAWAL D., BRUINING DH., *et al*. Adverse events associated with ERCP. *Gastrointest Endosc*., 2017, **85**: 32-47.
11. SUNDARALINGAM P., MASSON P., BOURKE MJ. Early Precut Sphincterotomy Does Not Increase Risk During Endoscopic Retrograde Cholangiopancreatography in Patients With Difficult Biliary Access: A Meta-analysis of Randomized Controlled Trials. *Clin Gastroenterol Hepatol.,* 2015,**13**: 1722-1729.e2.
12. NAVANEETHAN U., KONJETI R., VENKATESH PG., SANAKA MR., PARSI MA. Early precut sphincterotomy and the risk of endoscopic retrograde cholangiopancreatography related complications: An updated meta-analysis. *World J Gastrointest Endosc.*, 2014, **6**: 200-8.
13. LEE TH., BANG BW., PARK S-H., JEONG S., LEE DH., KIM S-J. Precut fistulotomy for difficult biliary cannulation: is it a risky preference in relation to the experience of an endoscopist? *Dig Dis Sci.*, 2011, **56**: 1896-903.
14. SAUKKO E., GRÖNROOS JM., SALMINEN P., HENNER A., NIEMINEN MT. Patient radiation dose and fluoroscopy time during ERCP: a single-center, retrospective study of influencing factors. *Scand J Gastroenterol*., 2018, **53**: 495-504.
15. RICHARDSON DB., CARDIS E., DANIELS RD., GILLIES M., O'HAGAN JA., HAMRA GB., *et al*. Risk of cancer from occupational exposure to ionising radiation: retrospective cohort study of workers in France, the United Kingdom, and the United States (INWORKS). *BMJ*., 2015, **351**: h5359.
16. HAYASHI S., NISHIDA T., MATSUBARA T., OSUGI N., SUGIMOTO A., TAKAHASHI K., *et al.* Radiation exposure dose and influencing factors during endoscopic retrograde cholangiopancreatography. *PloS One*., 2018, **13**: e0207539.
17. PASPATIS GA., ARVANITAKIS M., DUMONCEAU J-M., BARTHET M., SAUNDERS B., TURINO SY., *et al*. Diagnosis and management of iatrogenic endoscopic perforations: European Society of Gastrointestinal Endoscopy (ESGE) Position Statement - Update 2020. *Endoscopy*., 2020, **52**: 792-810.
18. PÉCSI D., FARKAS N., HEGYI P., VARJÚ P., SZAKÁCS Z., FÁBIÁN A., *et al*. Transpancreatic Sphincterotomy Is Effective and Safe in Expert Hands on the Short Term. *Dig Dis Sci.*, 2019, **64**: 2429-2444.