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Comparison of Early Needle-knife Precut Papillotomy over a Pancreatic Stent and Transpancreatic Sphincterotomy in Difficult Cannulation: A Prospective Randomized Controlled Trial

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Early NK Precut vs TPS in Difficult Cannulation: A RCT (ENKPT Trial)

Introduction

Selective bile duct cannulation is often required in therapeutic endoscopic retrograde cholangiopancreatography (ERCP). However, 10% to 20% of the bile duct remains inaccessible even by experienced endoscopists. [1, 2]
When standard methods of cannulation have been exhausted, the use of various precut techniques has been proposed to increase success rate. Needle-knife precut papillotomy (NKPP) is usually employed to facilitate access to the CBD in difficult cases. Most studies have identified precut and multiple cannulation attempts as two independent procedure- related risk factors for post-ERCP pancreatitis (PEP) [3, 4]. Furthermore, theand can significantly reduce the incidence of PEP in a randomized trial study [5]. NKPP with a small incision over a pancreatic stent will improve the success rate (96.9 % vs. 86.1 %, p = 0.0189)and reduces the complication rate (7.1% vs. 33.0 %, p < 0.001)comparing to standard NKP (without pancreas stent) [6]. Transpancreatic sphincterotomy (TPS), as an alternative method for bile duct entry when conventional biliary cannulation failed, has been documented with higher success rate of cannulation and similar complications. Although NKPP and TPS have been compared previously [7-12], randomized controlled trials on early NKP over a pancreatic stent comparing with TPS have been rare. The present prospective randomized controlled trial compared two kinds of methods in terms of success rate, cannulation time, and complications in the difficult cannulation.

Materials and methods

Patients and assessments

We will enroll ERCP-naïve patients between Nov. 2021 and Dec.2025 at Kaohsiung Chang Gung Memorial Hospital, Taiwan. Eligible participants were at least 20 years old. One experienced endoscopist (Dr. Liang), who conducted an average of 300 ERCPs per year, performed the procedures. The study exclusion criteria included previous sphincterotomy, peripapillary diverticula, active pancreatitis, Prior gastric surgery , Current use of antiplatelet agents, Coagulopathy , Peri-ampullary tumor related obstruction, pregnancy , Refused or were unable to give informed consent Also excluded were patients with successful CBD cannulation within 5 minutes of standard attempts and fewer than three passages of the guidewire into the mian pancreatic duct (MPD) (defined as “easy CBD cannulation”).We will gather written informed consent from all included patients before the trial. Before ERCP, we recorded the following demographic and clinical variables: age, sex, history of

coexisting comorbidities, alcohol consumption, smoking habits, American Society of Anesthesiologists (ASA) score, and serum levels of albumin, C-reactive protein (CRP), total bilirubin, prothrombin time (PT), activated partial thromboplastin time (APTT), pancreas and liver function enzymes, as well as a complete and differential blood counts obtained in the emergency room (ER) before and after ERCP for evaluation of complications. Additionally, endoscopic findings were recorded, including the time and frequency attempts of cannulation, papilla type [13], juxtapapillary diverticulum, and procedure methods used.

Study design

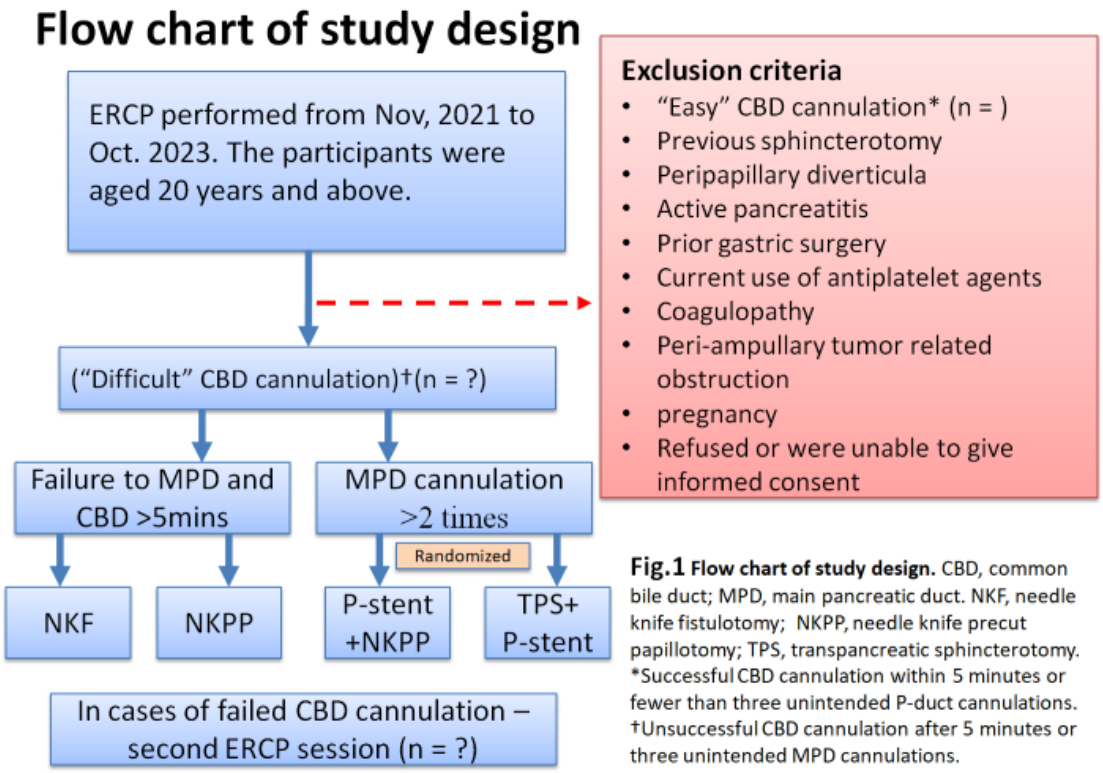

Fig.1 Flow chart of study design. CBD, common bile duct; MPD, main pancreatic duct. NKF, needle knife fistulotomy; NKPP, needle knife precut papillotomy; TPS, transpancreatic sphincterotomy. *Successful CBD cannulation within 5 minutes or fewer than three unintended P-duct cannulations. †Unsuccessful CBD cannulation after 5 minutes or three unintended MPD cannulations.

The "difficult CBD cannulation" was defined as unsuccessful CBD cannulation after 5 minutes (stopwatch count) or three passes of the guidewire into the MPD. If the patients with failure cannulation to CBD and MPD for more than 5 minutes were treated with needle knife precut papillotomy (NKPP group) or needle knife fistulotomy (NKF group) according to morphology of thepapilla of Vater [13]. If the patients with three passes of the guidewire into the MPD were randomly assigned, in a 1:1 ratio, to needle knife precut papillotomy following the pancreas stent placement (NKP-SIPS group) or tranpancreatic sphincterotomy followed by the pancreas stent placement (TPS group). A second ERCP was planned for 4–7 days

later for patients in whom ERCP failed. Patients are randomized into two groups at the time of providing informed consent by a 1:1 ratio, by opening a sealed envelope containing a noted marked with both groups. Individual random sequence is placed in an opaque envelop and kept by an independent research assistant who is not involved in this study.

Primary outcome was success rate of CBD cannulation. Secondary outcomes included the significant complications, including post-ERCP pancreatitis (amylase levels higher than three times the upper reference limit accompanied by abdominal pain)[14], perforation, and bleeding. Bleeding complications could present as melena or hematemesis, with a decrease in hemoglobin concentration of at least 2 g/dL. The definition of bleeding degree for patients who did not require transfusion was 'mild bleeding degree.' Cases requiring up to four units of blood were defined as 'moderate bleeding degree,' and those requiring five or more units of blood for transfusion, surgery, or angiography were defined as 'severe bleeding degree' [15]. Operation time during ERCP, defined as the period ranging from the beginning of cannulation to complete stone removal.

ERCP procedure

A side-view endoscope (JF-260V and TJF-240, Olympus Corp., Tokyo, Japan), a cholangiography catheter (PR-113Q, Olympus Corp., Tokyo, Japan), and a 0.035-in. Guidewires (*Jagwire*™ High Performance Guidewire; Boston Scientific, Natick, MA, USA) were used in the ERCP procedures. Endoscopic sphincterotomy (EST) was performed using standard pull-sphincterotomes (*ENDO-FLEX* GmbH, Voerde, Germany). In cases where biliary cannulation was difficult, we performed precut papillotomy or fistulotomy (Needle Knife, pointed type, *ENDO-FLEX* GmbH, Voerde, Germany) or transpancreatic sphincterotomy (TPS) [16]. EST was performed by using electrosurgical current generator Olympus ESG-100 (Olympus Optical Corporation, Tokyo, Japan). It was set on 20 W maximal output with pulse cut slow setting which cuts with alternating cutting and coagulation phase. The needle-knife precut techniques are freehand precut starting either from the papillary orifice (NKP) or at the papillary roof (needle-knife fistulotomy, NKF) after failure cannulation attempt to CBD and MPD for more than 5 minutes. If the papilla was treated with three unintended MPD cannulations, a needle-knife precut papillotomy with a small incision over a pancreatic stent (NKP-SIPS) [6] or TPS would be performed. With regard to NKP-SIPS, the direction of the incision is the same as that in NKP; pancreatic stent (Geenen Pancreatic Stent; Cook Medical,straight, 5 Fr/5 cm) is initially placed as a guide to facilitate biliary localization and to prevent post-ERCP pancreatitis; then, the incision is made starting at the papillary orifice, and,

proceeding in a layer-by-layer fashion, extended upward in 1–2-mm increments, but not beyond the oral protrusion, to a length of less than 5 mm until the underlying biliary sphincter was visualized. TPS was performed as Goff reported; in short, after cannulation of the pancreatic duct was achieved, a pull-sphincterotome on a guidewire was used to cut the septum between the bile and pancreatic ducts along the direction from 11 o'clock to 12 o'clock. After that, the pancreatic stent is placed first, and the sphincterotomy is extended to expose the biliary lumen, and the biliary duct can be cannulated.

A pancreas duct stent was placed for preventing post-ERCP pancreatitis (PEP) if the pancreas duct cannulation occurred twice or more. After ERCP, 50 mg of diclofenic was administered anally to all patients who did not have a history of allergy [18]. Aggressive intravenous hydration (including 3 mL/kg/h during ERCP, a 20-mL/kg bolus, and 3 mL/kg/h for eight hours after ERCP) with lactated Ringer's solution was administered to all patients without contraindications [19]. CBD stones were extracted using a balloon and/or basket catheter. A retrograde biliary drain with a plastic stent (ERBD) was inserted if CBD stone extraction could not be performed within one hour of the procedure, if the contrast medium bile flow was poor with papilla swelling after stone extraction, or if pus bile was noted. All patients underwent empiric antimicrobial treatment for acute cholangitis. All patients were asked to fast for at least 12 hours after ERCP and received intravenous proton pump inhibitors (PPIs) two doses, and then shifted to oral PPIs once daily for seven days.

Block randomization

Patients were distributed on one block with 4 numbers and each group contained two numbers (A, B). The admitted patients who were eligible for inclusion were given numbers in the order; number A was allocated to (P-stent + NKPP group) as the study group and patient who carried number B was allocated to (TPS+ P-stent group). So, the study and control groups were randomized into 1:1.

Statistical analysis

Descriptive statistics, including distribution, absolute frequency, relative frequency, medians with range, and means ± standard deviation (SDs) were calculated depending on the variable type. Between-group differences for quantitative variables with normal distribution were compared using Student's *t*-test. The differences between categorical data proportions were evaluated with Fisher's exact test when there were fewer than five expected cases; otherwise, we used the chi-square test. We included factors with probability (p) values < 0.05 in the univariate analysis in the logistic regression analysis. A multivariate logistic regression model was adopted to

identify independent factors of procedural success and major adverse events. A *p* value < 0.05 was considered to indicate statistical significance in all analyses.

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Chang Gung Memorial Hospital, Kaohsiung Branch

Chang Gung Medical Foundation

Informed Consent Form

I. Comparison of Early Needle-knife Precut Papillotomy over a Pancreatic Stent and Transpancreatic Sphincterotomy in Difficult Cannulation: A Prospective Randomized Controlled Trial

II. Basic Study Information

Medical Record Number: _____

1. **IRB Approval Number: IRB 202101221A3**
2. **Study Site:** Chang Gung Memorial Hospital, Kaohsiung Branch
3. **Department Responsible for Execution:** Division of Gastroenterology and Hepatology
4. **Sponsoring Organization / Company:** Chang Gung Hospital Research Project
5. **Principal Investigator:** Dr. Hui-Ming Su
   Affiliation: Division of Gastroenterology and Hepatology
   Title: Attending Physician (Lecturer Level)
   Phone Number: 0975-353-218

Co-Principal Investigator: Dr. Yi-Chun Chiu
Associate Investigators: Dr. Chung-Mou Kuo, Dr. Chih-Ming Liang, Dr. Lung-Sheng Lu, Dr. Chen-Kun Wu
Affiliation: Division of Gastroenterology and Hepatology
Titles: Attending Physicians (Associate Professor Level, Assistant Professor Level, and General Attending Level)
Phone Number: +886-7-731-7123 ext. 2444
Emergency Contact Number for Participants: 0975-056-294

6. **Participant's Name:**
   Participant Study ID Number:
   Gender:
   Date of Birth:
   Mailing Address:
   Contact Phone Number:

III. Introduction

Hello,

Therapeutic endoscopic retrograde cholangiopancreatography (ERCP) is the standard treatment for conditions such as cholangitis, bile duct stones, and obstructive jaundice. However, even in the hands of experienced endoscopists, successful bile duct cannulation may still fail in 10%–20% of cases. When standard cannulation techniques are unsuccessful, various precut techniques are recommended to improve the success rate.

Early needle-knife precut sphincterotomy (performed after 5 minutes of failed cannulation) has been shown to be an effective method. A randomized clinical trial demonstrated that early use of this technique significantly reduced the incidence of post-ERCP pancreatitis. Compared to standard precut sphincterotomy without pancreatic duct stenting, using a small incision precut sphincterotomy over a pancreatic stent can further increase the success rate and reduce complication risks.

Another approach, transpancreatic sphincterotomy, has also proven to yield high cannulation success rates with comparable complication rates. While previous studies have compared precut sphincterotomy and transpancreatic sphincterotomy, randomized controlled trials evaluating early use of both techniques with pancreatic duct stenting remain rare. For this reason, further investigation is warranted.
Before you agree to participate in this study, your physician will explain the content of this informed consent form. Please read it carefully and ask any questions you may have. Participation in the study is completely voluntary, and choosing not to participate will not affect your legal rights to receive appropriate medical care.

IV. Purpose of the Study

To compare, in cases of difficult cannulation, the differences in success rate, cannulation time, and complication rate between early needle-knife precut sphincterotomy over a pancreatic stent and transpancreatic sphincterotomy.

V. Inclusion and Exclusion Criteria

Inclusion Criteria:

You are eligible to participate in this study if all of the following conditions are met:

1. Willing to sign the written informed consent form.
2. Male or female patients aged 20 years or older.
3. Undergoing ampullary treatment for the first time.

Exclusion Criteria:

You will not be eligible to participate in this study if any of the following conditions apply:

1. Currently using non-steroidal anti-inflammatory drugs (NSAIDs), including aspirin, Pletaal (cilostazol), or have known coagulopathy.
2. Biliary or gastroduodenal strictures caused by tumors.
3. Tumors or diverticula located near the ampulla of Vater.
4. History of prior abdominal surgery resulting in altered intestinal anatomy.
5. Acute pancreatitis.
6. Pregnancy.
7. Evidence of severe infection, such as respiratory distress or unstable blood pressure—indicators of a serious systemic infection.

VI. Study Methods and Procedures

We will recruit approximately 400 treatment-naïve patients requiring therapeutic biliary endoscopy at Chang Gung Memorial Hospital, Kaohsiung, Taiwan, from November 2021 to October 2023. Eligible participants must be at least 20 years old.

"Difficult biliary cannulation" is defined as failure to achieve successful bile duct cannulation after 5 minutes (measured with a stopwatch) or after guidewire insertion into the pancreatic duct on three occasions.

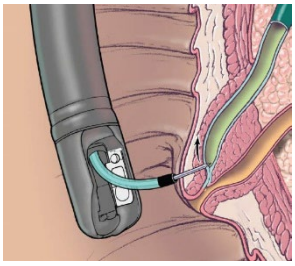
Patients who fail both bile and pancreatic duct cannulation after 5 minutes will be assigned to one of two treatment groups based on the morphology of the ampulla:

- Needle-knife precut sphincterotomy group
- Needle-knife fistulotomy group

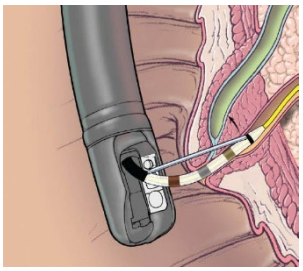
Patients in whom the guidewire enters the pancreatic duct two times will be randomized in a 1:1 ratio to either:

- Needle-knife precut sphincterotomy after pancreatic stent placement, or
- Transpancreatic sphincterotomy followed by pancreatic stent placement.

Needle-knife precut sphincterotomy



Transpancreatic sphincterotomy



VII. Potential Risks, Side Effects, Incidence Rates, and Management

Based on previous studies, the reported risks and complications for each technique are as follows:

Transpancreatic Sphincterotomy

- Pancreatitis: 10.4%
- Bleeding: 0–1%
- Intestinal perforation: 0–1%
- Mortality: 0–0.5%

Needle-Knife Precut Sphincterotomy

- Pancreatitis: 6.1%
- Bleeding: 0–1%
- Intestinal perforation: 0–2%
- Mortality: 0–0.5%

For participants enrolled in this study, the placement of a pancreatic duct stent may reduce the risk of post-procedural pancreatitis by approximately 50%. However, in very rare cases, the stent may migrate proximally, which may require additional endoscopic or surgical intervention for removal.

After the procedure, you will be asked to fast until the following day. During this period, medical staff will closely monitor for abdominal pain and vital signs. Patients who underwent painless (sedated) endoscopy will also be observed for full recovery of consciousness after returning from the recovery room.

If you experience symptoms such as abdominal bloating, pain, melena (black stool), fever, or confusion, please immediately inform a healthcare provider. If no such symptoms are present the following day, you may begin drinking water, followed by a soft or liquid diet.

Management Procedures:

1. If you experience any discomfort, please inform your attending physician. They will provide you with the most appropriate care and treatment.
2. In the event of an emergency or any unusual symptoms that cannot be controlled

with standard medical treatment, please contact your physician **Dr. Chih-Ming Liang** at **0975-056-294** or the research staff at **07-342-2121 ext. 2444** immediately.

VIII. Alternative Treatment Options

Therapeutic endoscopic retrograde cholangiopancreatography (ERCP) is the standard treatment for cholangitis, bile duct stones, and obstructive jaundice.

If you choose not to participate in this clinical trial, your physician will still provide appropriate treatment based on their clinical experience and the condition of your ampulla. For example, some physicians may be more experienced with **needle-knife precut sphincterotomy** than with **transpancreatic sphincterotomy**, and may therefore choose the technique with which they are more familiar.

IX. Contraindications and Restrictions Related to This Study

This study will be conducted in accordance with routine follow-up visits and standard medical care. You are **not required to comply with any additional restrictions** beyond your usual care. However, if any **unexpected surgical procedures** are needed, they should be discussed with your physician and properly documented.

X. Expected Outcomes of the Study

The early application of the two techniques, in combination with pancreatic duct stenting, **may reduce overall complication rates**. However, further research is still needed to confirm this potential benefit.

XI. Emergency Management

If you experience any discomfort or adverse symptoms during the study, please inform your **study physician** immediately. Your doctor will make every effort to provide the most appropriate care and treatment.

In the event of a **medical emergency** or **unusual physical condition** that cannot be effectively managed with standard medication, please contact your **attending physician** or the **Principal Investigator**, **Dr. Chih-Ming Liang (Division of Gastroenterology and Hepatology)**, at his **24-hour emergency contact number: 0975-056-294**, or contact the study staff at **+886-7-731-7123 ext. 2444**.

XII. Compensation, Cost Responsibility, and Injury Reimbursement

1. **Compensation:**
   There is **no monetary compensation** provided for participation in this study.
2. **Cost Responsibility:**
   This study is funded by research grants from Chang Gung Memorial Hospital. Under Taiwan's National Health Insurance system, **you will not incur any additional costs** for participating in this study.

(1) If an adverse event or injury occurs as a direct result of procedures conducted according to the study protocol, the hospital and the principal investigator will bear legal responsibility for providing compensation, **except for adverse events that are already listed as foreseeable in this consent form**, which will not be eligible for compensation.

(2) In the event of an adverse reaction or injury related to this study, **professional medical care and consultation will be provided at no cost to you**.

(3) Aside from the above-mentioned compensation and medical care, **no additional compensation will be offered**. If you are not comfortable with this level of risk or arrangement, you are advised **not to participate in this study**.

(4) Signing this informed consent form **does not waive any of your legal rights**

XIII. Privacy and Confidentiality Protection

1. A unique **research code** will be assigned to represent your identity. This code will **not contain your name, national ID number, or address**.
2. All diagnostic information and study findings will be handled with strict confidentiality by the principal investigator. If research results are published, **your personal identity will not be disclosed**.
3. By signing this consent form, you agree that your research records may be directly accessed by authorized monitors, auditors, the Research Ethics Committee (IRB), and regulatory authorities **to ensure compliance with applicable laws and regulations**. These individuals are obligated to **maintain the confidentiality of your personal information**.

XIV. Withdrawal and Discontinuation from the Study

You, or your legal representative, **have the right to withdraw from this study at any time and for any reason** without affecting your medical care or legal rights.

Additionally, the **principal investigator may terminate your participation** or halt the study if necessary.

XV. Subject Rights

1. The collection, processing, and use of your personal data will be handled by the study institution and investigators in accordance with this informed consent form, relevant clinical trial regulations, and the **Personal Data Protection Act** of Taiwan. You may exercise the following rights in writing by contacting the study institution or investigator:

(1) Request to access or review your personal data;
(2) Request a copy of your personal data;
(3) Request to supplement or correct your personal data;
(4) Request to stop the collection, processing, or use of your personal data;
(5) Request deletion of your personal data.

2. During the course of the study, you will be promptly informed of any significant new findings that may affect your willingness to continue participation. If you have any questions or concerns during the study, please contact the principal investigator.
3. If you have questions about your rights as a research participant or believe that you have been harmed by participating in this study, you may contact the **Institutional Review Board (IRB)** of this hospital for consultation at:
   (03) 319-6200 ext. 3703, 3705–3709, 3711–3717

XVI. Ownership of Study Results and Benefits

If the results of this study lead to academic publications, tangible benefits, or other related outcomes, you agree that such outcomes may be donated **free of charge** to this hospital for **public interest purposes**, such as disease prevention, diagnosis, and treatment.

XVII. Storage and Reuse of Personal Data, Samples, and Derivatives

This study **does not involve any leftover biological samples** for future storage or reuse.

XVIII. Declaration

The contents of this study and the informed consent form have been **fully explained orally** to the participant by _____. The participant and/or their legal representative has fully understood and agrees to participate in the study.

This consent form is made in **duplicate**, and a **copy has been provided to the participant**.

Signatures

A. Participant:

Name (Print): _____

Signature: _____

Date: ____ / ____ / _____ (YYYY/MM/DD)

B. Person Obtaining Consent:

Name (Print): _____

Signature: _____

Date: ____ / ____ / _____ (YYYY/MM/DD)

C. Co-Investigator / Associate Investigator:

Name (Print): _____

Signature: _____

Date: ____ / ____ / _____ (YYYY/MM/DD)

D. Principal Investigator:

Name (Print): _____

Signature: _____

Date: ____ / ____ / _____ (YYYY/MM/DD)

(*Required if the participant meets the condition described in Section I of the Consent Signing Instructions*)

E. Legal Representative / Authorized Consenter / Guardian / Conservator:

Name (Print): _____

Signature: _____

Date: ____ / ____ / _____ (YYYY/MM/DD)

Relationship to the Participant: _____

(*Required if the participant meets the condition described in Section II of the Consent Signing Instructions*)

F. Witness:

Name (Print): _____

Signature: _____

Date: ____ / ____ / _____ (YYYY/MM/DD)

[Chang Gung Medical Foundation / Chang Gung University / Chang Gung University of Science and Technology – Information for Research Participants]

Dear Participant, Family Member, or Member of the Public,
If you meet the eligibility criteria for a clinical trial or research study, you may be invited to participate in a study conducted by Chang Gung Memorial Hospital, Chang Gung University, or Chang Gung University of Science and Technology. The following information is provided to protect your safety and rights as a research participant. It explains the role and responsibilities of the **Institutional Review Board (IRB)** at Chang Gung Medical Foundation, how research is reviewed, and what your rights are as a participant.

What is Research?
Research is different from treatment.
Treatment involves procedures and medications that have already been studied and are known to have predictable outcomes and side effects. Research, on the other hand, aims to discover new knowledge and often involves **uncertainty about outcomes**. Participation in research is **completely voluntary**, and choosing not to participate **will not affect your right to receive medical care** or result in any form of unfair treatment.

What is the Institutional Review Board (IRB)?
The **Institutional Review Board (IRB)** is a committee established to ensure that research involving human participants is **scientifically and ethically appropriate**. It is composed of medical professionals, legal experts, community representatives, and members of non-medical backgrounds who help researchers understand the concerns of participants to ensure their safety and rights are protected.
If you have any questions about your rights, you may contact the IRB of Chang Gung Medical Foundation.

How Does the IRB Review Clinical Trials or Research Studies?
1. **All research conducted at Chang Gung Memorial Hospital, Chang Gung University, or Chang Gung University of Science and Technology must be reviewed and approved by the IRB** before it can begin.
2. Research protocols submitted to the IRB are independently and professionally reviewed by committee members and experts.
   The review focuses on whether participants are fully informed about the study — including:
   - The purpose of the study
   - The procedures involved
   - Possible alternative treatments
   - Potential risks, side effects, and benefits
   - How to withdraw from the study
   - How privacy and confidentiality will be protected
3. During review, the IRB evaluates **potential risks** to participants, which may include:
   - Physical discomfort or harm
   - Psychological stress
   - Social or financial impact

The IRB ensures that all **risks are minimized** and justified by the **potential benefits** — either to the participant, or to future patients through scientific knowledge.
Studies that pose high risk with **no reasonable benefit** will **not be approved**.

4. After a study is approved, the IRB and the research institution will **continue monitoring the research** to ensure that it is carried out exactly as approved and that participants' rights and safety remain protected.

What Are Your Rights as a Research Participant?

- **Right to Be Informed**

You have the right to clear and complete information about:

1. **Purpose of the study**
   The researcher must explain the aim of the study in simple and understandable language.
2. **What will happen during the study**
   You should know what procedures will be involved, how often visits occur, whether blood samples will be taken, and any inconvenience to your daily life.
3. **Alternative treatment options**
   You have the right to know about other treatments available if you choose not to participate.
4. **Risks and side effects**
   All research involves risk. You must be informed of potential risks and side effects, and what to do in case of an emergency — including who to contact and who will provide follow-up medical care and cover related costs.
5. **Potential benefits and expected outcomes**
   Researchers must explain any direct benefits to you, or how the study may help others in the future through new discoveries.
6. **How to withdraw from the study**
   You must be informed about how to withdraw at any time, what happens to your data after withdrawal, and whether follow-up care is available.
7. **Freedom to ask questions**
   You may ask the research team questions **at any time**.

- **Right to Voluntary Participation**

You will only officially become a participant **after the researcher explains** the study purpose, procedures, risks, benefits, and your rights, and **after you sign the informed consent form** of your own free will.
You may also **withdraw at any time** without giving a reason.
Your decision to withdraw will **not affect your future medical care** or cause you to be treated unfairly.

- **Right to Protection**

1. **Privacy and confidentiality**
   Any personal information collected during the study will be kept confidential. If study results are published, or reviewed by the IRB or regulatory agencies (e.g., the Ministry of Health and Welfare), **your identity will not be revealed**.
2. **Retention of your legal rights**
   Participation in a clinical study does **not mean you give up any legal rights** you currently have

Chang Gung Medical Foundation

Institutional Review Board

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REPUBLIC OF CHINA

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Date 2021/09/28

Protocol Title: Comparison of Early Needle-knife Precut Papillotomy over a Pancreatic Stent and Transpancreatic Sphincterotomy in Difficult Cannulation: A Prospective Randomized Controlled Trial.

IRB No.: 202101221A3

Principal Investigator(s): SOU, FAI-MENG

Co-Investigator(s): CHIU, YI-CHUN, KUO, CHUNG-MOU,LIANG, CHIH-MING,MA, TE-LING,LU, LUNG-SHENG,WU, CHENG-KUN

Executing Institution: Kaohsiung

Duration of Approval: From 2021/11/1 To 2022/10/31

Version/Date of documents:

(1)Protocol: 2021/09/01 version2

(2)Chinese Synopsis: 2021/09/01 Version2

(3)Informed Consent Form: 2021/09/27 Version4

(4)Case Report Form: 2021/07/19 Version1

Date of Meeting: 2021/09/15

Date of Approval: 2021/09/28

Frequency of Continuing Report: Once a year

※Next Deadline of Continuing Report: 2022/10/31. To facilitate the review, please submit the report two months before the deadline (or one month before the expiration of the trial if a continuing report shall be provided every three months) in order not to influence the principal investigator's right to conduct the research. In the case that failure or delay to submit a continuing report makes the IRB unable to determine the next trial period by the deadline, the trial shall not be continuously conducted.If the Principal Investigator fails to submit a continuing report on time, rendering the Institutional Review Board unable to issue the next trial execution period before the previous trial execution period expires, all research activities, including the intervention or interaction with

the participating trial subjects, must be suspended. Unless the Institutional Review Board considers that the continuation of trial intervention or trial participation is greatly beneficial to the trial subject's safety or in the best interest of the trial subject from a moral point of view, no new trial subject shall be included until the continuing report is formally approved.

The IRB is organized and operates in accordance with Good Clinical Practice and the applicable laws and regulations.

T. T. Hsieh

Tsang-Tang Hsieh,MD
Chairman
Institutional Review Board
Chang Gung Medical Foundation