Informed consent
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Informed Consent for Extended pancreatic neck transection versus conventional pancreatic neck transection during laparoscopic pancreaticoduodenectomy (LPDEXCEPT): a multicenter superiority randomized controlled trial

Informed page

Dear Mrs. /Mr.,

Thank you for your interest in our clinical research! We will invite you to participate in a randomized controlled clinical trial of extended pancreatic neck transection versus conventional pancreatic neck transection during laparoscopic pancreaticoduodenectomy (LPDEXCEPT).

Before you decide whether to participate in this study, please read the following as much as possible to help you understand the research, the purpose, the research process, and deadlines, and what may be brought after you participate in this study, which might be benefits, risks or discomfort. If you prefer, you can also discuss it with your family, friends, or ask your doctor for an explanation.

This clinical trial has been approved by the Ethics Committee on Biomedical Research of West China Hospital of Sichuan University (2023-167) in March 2023. And the number of participants in this study is expected to be 154.

I. Why to participate in this trial? (Research background and research purposes)

Pancreaticoduodenectomy is the standard procedure for patients with malignant or benign tumors of the pancreatic head, the lower common bile duct, and the periampullary area of the duodenum. Since Gagner and his colleagues performed and introduced the first total laparoscopic pancreaticoduodenectomy (LPD) in 1994, LPD has become progressively acknowledged for its advantages such as less bleeding, less pain, and faster recovery.

Despite the advances in laparoscopic technology, postoperative pancreatic fistula (POPF) remains one of the most severe complications of LPD, which occurs in around 20% of patients. POPF is typically associated with secondary complications, such as post-pancreatectomy hemorrhage, intra-abdominal infection. These could lead to prolonged length of hospital stay, increased hospital cost, and even death. Therefore, prevention of POPF has always been of high priority in pancreatic surgery.

The level of pancreatic neck transection during LPD is not conclusive. Theoretically, the level of pancreatic transection can significantly affect the occurrence of POPF by influencing both the blood supply to the anastomosis and the location of the main pancreatic duct in the pancreatic transverse section. The head of the pancreas is supplied by the anterior and posterior pancreaticoduodenal arterial arcades which are formed by branches from the celiac trunk and the superior mesenteric artery. The body and tail of the pancreas are supplied by branches from the splenic artery. And there is an intermediate zone lacking proper vascularization in the neck of the pancreas, called “vascular watershed”. Therefore, the level of pancreatic neck transection might influence the pancreatic stump vascularization. Strasberg and his colleagues have studied the impact of the defects of pancreatic stump vascularization on POPF and showed there is a statistically significant correlation. The main pancreatic duct arises in the tail of the pancreas, and lies midway between the superior and inferior margins and slightly more posterior than anterior through the tail and body of the pancreas. Then it

turns caudad and posterior on reaching the head of the pancreas. Therefore, the level of pancreatic neck transection could influence the location of the main pancreatic duct in the pancreatic transverse section. Angzhi Li and his colleagues have studied the impact of the location of the pancreatic duct on POPF. And they found the risk of POPF was reduced when the center of pancreatic duct is far from the edge of pancreas.

Bardol and his colleagues conducted a retrospective cohort study and consolidated that a long remnant pancreatic neck could be an independent risk factor for POPF after pancreaticoduodenectomy. However, to date, there exists no randomized study dedicated to answering whether patients could benefit from extended pancreatic neck transection during LPD. Thus, we conduct a multicenter randomized trial, LPDEXCEPT, with the hypothesis that extended pancreatic neck transection has superiority to conventional pancreatic neck transection.

The broad goal of this trial is to evaluate the superiority of extended pancreatic neck transection during LPD.

II. What will be done if you participate in the research?

If you meet the inclusion criteria and agree to participate, you will be tested according to the following steps: divided into two groups according to the study plan, respectively, undergoing extended pancreatic neck transection or conventional pancreatic neck transection during LPD. You may be assigned in any group. All patients underwent routine nursing of biliary and pancreatic surgery, and collected various indexes before, during and after surgery. At the same time, follow-up for 3 months. The time points of follow-up were the first and third month postoperatively. The follow-up method was ward follow-up combined with telephone follow-up.

III. What are the alternative treatment options?

Patients with resectable benign or malignant tumors of the lower common bile duct, periampullary region of the duodenum, and head of the pancreas could participate in this trial. Alternative treatment options for patients with benign tumors include regular follow-up with conservative observation. According to the existing guidelines, surgical resection is preferred for patients with resectable malignant tumors, and no other treatment alternatives are recommended.

IV. Who can participate in this study? Who is not suitable for research?

Who can:

(1) Patients with benign or resectable malignant tumors of the lower common bile duct, Vater ampulla, head or uncinate process of the pancreas.
(2) 18 years old < age < 80 years old, no gender limit.

(3) Patient is expected survival beyond 3 months.
(4) No pregnancy or pregnancy plan within 3 months after surgery.
(5) Nutrition risk score <3 according to the Nutritional Risk Screening for Inpatients 2002 (NRS2002) standard score.
(6) No contraindication to surgery for anesthetic evaluation.
(7) The subjects voluntarily joined the study and signed an informed consent form, with good compliance and cooperation with follow-up.

Who not:

(1) Patients with borderline resectable and unresectable malignancies.
(2) Patients undergoing neoadjuvant chemotherapy or radiotherapy.
(3) Patients with tumors exceeding the level of the gastroduodenal artery as measured by preoperative radiography.
(4) Intraoperative exploration reveals tumor adhesions with portal vein-superior mesenteric vein, requiring revascularization and reconstruction.
(5) Operation transfers to open.
(6) Operation transfers to other procedure.

V. Adverse reactions, risks, and protective measures for participating in the study.

The main adverse reactions and risks are as follows:

1. In the operation, the surgical method is determined according to medical conditions according to the condition.
2. Due to the patient's condition (critical, complicated, poor systemic conditions), individual differences, sudden and sudden recession may occur during and after surgery, multiple organ failure (such as heart failure, respiratory failure, liver failure, renal function) Failure, DIC, etc.) or unpredictable changes in the condition can be life-threatening.
3. Major bleeding, hemorrhagic shock may occur during surgery, and life-threatening.
4. The operation is due to anatomical variation and severe adhesion for therapeutic purposes. It may be inevitable to damage surrounding and nearby tissues and organs, and the corresponding organs need to be repaired or reconstructed.
5. Special medical supplies such as chemotherapy pumps, anastomotic devices, etc. may be used during surgery, and special treatments such as radiofrequency therapy and cryotherapy may be used during surgery.
6. Tumor patients may not be able to undergo surgical resection due to the condition, or recurrence and metastasis after resection, requiring further treatment.
7. Recurrent bleeding after surgery, local, systemic infection, bile leakage, pancreatic leakage, intestinal leakage, anastomotic leakage, and other changes in the condition may be life-threatening and require reoperation if necessary.
8. Other unforeseen or unpredictable adverse consequences and medical risks.
9. May need to be admitted to the ICU ward, if necessary, after surgery.
10. Postoperative examination may be inconsistent with preoperative diagnosis and intraoperative diagnosis. The final diagnosis is based on postoperative examination.

11. Determine the risk of biopsy of the lesion under the endoscope under the condition of the operation.
12. During the operation, malignant tumor metastasis is found, and it is difficult to cure radically or radically. The risk of radical resection is great. Only palliative anastomosis is possible.
13. During the operation, the abdominal cavity is widely metastasized, and it is impossible to perform resection or palliative anastomosis.
14. Postoperative abdominal adhesions, intestinal adhesions, intestinal obstruction, may require relevant treatment.
15. Long-term bed rest, pulmonary infection, and deep vein thrombosis may occur.
16. Incision healing may occur after surgery, infection of the incision, incision splitting, incisional hernia, etc.
17. Pancreatic exocrine insufficiency.
18. Laparoscopic pancreaticoduodenectomy may be due to tissue adhesion, intraoperative bleeding, etc.
19. Pneum abdominal syndrome, etc.

VI. What will be done in the event of any of these adverse events during the study?

If there is any discomfort in the study, or the condition changes, or any unexpected situation, regardless of whether it is related to treatment, you should promptly notify your doctor, he/she will make an accurate judgment and medical treatment. deal with. If the patients participating in the trial have the above complications, they will form a professional medical team to deal with and treat them for the first time. If an adverse event occurs in a clinical trial, the Medical Expert Committee will determine if it is related to surgery or trial. The treatment and examinations required for other diseases that you have combined at the same time will not be included in the free range.

VII. Possible benefits of participating in the Study.

By participating in this study, your condition may improve. And the study may help determine which treatments are safer and more effective in treating other patients with conditions like yours.

VIII. The relevant costs.

Subjects will not pay for participation in this trial, except for the costs incurred during the treatment.

IX. The confidentiality of clinical data.

Your medical records (research medical records, CRF, test results, etc.) will be kept completely at

the hospital where you are attending. The doctor will record the results of the tests and other tests on your medical record. Researchers, ethics committees, and higher-level medical administrations will be allowed to access your medical records. Any public report about the results of this study will not disclose your personal identity. We will make every effort to protect the privacy of your personal medical information to the extent permitted by law. According to medical research ethics, in addition to personal privacy information, experimental data will be available for public inquiry and sharing. Query and sharing will be limited to web-based electronic databases, ensuring that no personal privacy information will be disclosed.

X. Do you have to participate in the trial?

Whether or not to participate in the research is entirely up to you. You may decline to participate in the study or withdraw from the study at any time during the study, which will not affect your relationship with the doctor and will not affect your medical or other benefits.
For your best interest, your doctor or researcher may discontinue your participation in this study at any time during your research.

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Signature page

Clinical Research Project: Extended pancreatic neck transection versus conventional pancreatic neck transection during laparoscopic pancreaticoduodenectomy (LPDEXCEPT): a multicenter superiority randomized controlled trial.

Research Center Name:_____

Subject's Statement: I have carefully read the contents of the informed consent form, and the researchers have answered my questions. I fully participated in the study and fully cooperated with the researcher after fully understanding the purpose, method, possible therapeutic benefits and possible risks and other provisions mentioned in the informed consent form. I understand that I can withdraw from the study at any time, and I do not need any reason. The medical services I receive and the legal rights I enjoy are not affected at all. Finally, I decided to agree to participate in this study and to ensure compliance with my doctor's advice.

Subject Signature:_____

Date:_____

Contact Number:_____

Subject's Legal Agent signature (If applicable):

Date:_____

Contact Number:_____

Doctor's Statement: I have explained fully detail to the subjects, including the potential risks.

Doctor Signature:_____

Date:_____

Contact Number:_____

Ethics Committee on Biomedical Research of West China Hospital of Sichuan University
Contact Number:028-85422654，028-85423237

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探究腹腔镜胰十二指肠切除术中胰颈离断位置与术后胰瘘发生的相关性关系
临床研究知情同意书

尊敬的受试者

我们邀请您参加四川大学华西医院批准开展的“探究腹腔镜胰十二指肠切除术中胰颈离断位置与术后胰瘘发生的相关性关系”课题研究。本研究将在贵州医科大学附属医院、攀枝花中心医院、山东省立医院、复旦大学附属肿瘤医院、广东省中医院、乐山市人民医院、云南省第一人民医院、常州市第一人民医院、齐鲁医院、南方医院等医院共同开展，估计将有 184 名受试者自愿参加。本研究已经得到四川大学华西医院生物医学伦理审查委员会的审查和批准。

1. 为什么要开展本项研究？

胰十二指肠切除术是治疗胰腺头部、胆总管下段及十二指肠壶腹周围肿瘤的标准术式。随着微创外科理念的不断发展，腹腔镜胰十二指肠切除术由于具有创伤小、出血量少、恢复快、疼痛轻等优势而得以发展。

胰瘘是 LPD 术后常见的并发症。探究 POPF 发生相关性因素，从而精准预防和管理 POPF、降低 POPF 发生率是胰腺外科领域主要研究内容。

目前导管对黏膜是学界广泛接受的胰肠吻合方式，手术操作时须将胰颈切缘面的主胰管和小肠黏膜进行缝合，既往相关研究表明主胰管在胰颈切缘面的位置是影响手术时吻合操作的因素之一，主胰管是否在切缘中央与术后是否发生 POPF 相关。主胰管在胰腺不同部位的走行位置不同：在胰腺体尾部，主胰管走行于胰腺的中间；从胰腺体部向胰腺头部的过程中，主胰管走行方向逐渐偏向足侧和后侧。因此，LPD 手术过程中，离断胰腺颈部的位置决定了主胰管在胰腺切缘断面的位置。

胰腺各部分动脉血供不同：胰腺头部的血供主要由胃十二指肠动脉发出的胰十二指肠上动脉和肠系膜上动脉发出的胰十二指肠下动脉形成的胰十二指肠前后动脉弓完成；胰腺体尾部的血供主要由脾动脉发出的数支分支完成。胰腺颈部血供由胰背动脉完成，而该动脉常存在变异和缺失，因此胰腺颈部常存在一段乏血供区。因此，在 LPD 术中，离断胰腺颈部的位置也影响胰腺切缘面血供是否充足。

综合上诉两方面原因，LPD 术中离断胰腺颈部的位置在学界存在争议。既往一份回

顾性研究表明，在距离肠系膜上静脉-门静脉左侧缘 7mm 处离断胰腺颈部是 POPF 的保护性因素。但该结论有待进一步前瞻性随机对照试验研究证实。

因此，本研究项目拟通过开展回顾性及前瞻性两部分研究工作探究腹腔镜胰十二指肠切除术中胰颈离断位置与术后胰瘘发生的相关性关系。

2. 如果参加研究，您需要做什么？

您首次住院期间除常规诊疗过程外无特殊额外工作。首次手术后 3 月内需按医生要求进行随访。受试期间，您可能随机被分配到对照组和实验组。对照组在 LPD 术中将在门静脉-肠系膜上静脉正前方离断胰腺颈部；实验组 LPD 术中将在门静脉-肠系膜上静脉左侧缘 0.5-1.0cm 处离断胰腺颈部。

3. 可供选择的诊疗方案有哪些？

患者为可切除的胆总管下段、十二指肠壶腹周围、胰腺头部良恶性肿瘤。其中良性肿瘤患者可选择的其他诊疗方法包括：定期随访保守观察治疗。依据现有指南，可切除的恶性肿瘤患者首选手术切除，无其他诊疗方法推荐。

4. 哪些人不宜参加研究?

如果您为 1）临界可切除及不可切除恶性肿瘤患者 2）行新辅助放化疗患者 3）术前影像学判断肿瘤超过胃十二指肠动脉水平患者 4)术中探查发现肿瘤与门静脉-肠系膜上静脉粘连，需行血管切除重建患者 5）术中中转开腹患者 6）术中探查后转行其他手术方式患者，则不宜参加本研究。7）根据《住院患者营养风险筛查 2002（NRS2002）》标准评分，营养风险评分＜3 分。

5. 参加研究有哪些风险？

参加研究，患者将面临行腹腔镜胰十二指肠切除术常规面临的麻醉风险及手术风险，具体包括：

A. 麻醉风险

1）麻醉过程中可能进行以下某一项或多项操作，包括气管插管、椎管内穿刺、周围神经阻滞、深静脉穿刺置管术、动脉穿刺置管术、喉罩插入、气管切开术、气管和支气管镜检查、食管超声波检查、有创血液动力学监测等。这些操作均可能引起组织出血、神经损伤、创伤、感染、坏死等。

2）根据麻醉操作常规，按照《中华人民共和国药典》要求使用各种、各类麻醉药后，病人可能出现中毒、过敏、高敏、神经毒性等反应，导致休克、严重脏器功能损害、呼吸心跳停止，甚至生命危险。已麻醉时，特别是急症和饱腹病人发生胃内容物反流、误吸、喉痉挛、呼吸道梗阻、神经反射性休克和心律失常等而致重要脏器功能损害，危及生命。

3）气管插管可引起牙齿脱落、口唇、舌、咽喉、声带、气管和支气管损伤，喉痉挛、气管痉挛、支气管痉挛及功能损害。气管插管困难通气不能维持时，可能需要进行紧急气管切开术，缺氧时可危及生命。

4）椎管内麻醉及区域麻醉发生神经、血管、脊髓等组织结构损伤，可能出现全脊髓麻醉、截瘫、椎管内感染、血肿、腰痛、头痛、肢体伤残、甚至呼吸心跳停止等危及生命。

5）患者本身合并其他疾病或有重要脏器损害者，相关并发症和麻醉危险性显著增加。

6）麻醉方法的选择和改变由实施麻醉的医师根据病情和手术的需要决定。 7）可能发生术中知晓和术后回忆。

8）其它发生率极低或难以预料的意外和并发症，以及其它不可预料的不良后果。

9）麻醉手术中输血输液可能发生致热源反应、过敏反应、血源性传染病等。

B. 手术风险

1）术中损伤神经、血管及邻近器官，如：脾、胃肠道、肾脏、肾上腺等。

2）术中大出血，导致失血性休克，严重者死亡（脾动/静脉、门静脉损伤）。

3）伤口积液、血肿、感染、裂开、延迟愈合或不愈合，瘘管及窦道形成，切口疝。

4）术后乳糜瘘，需长时间保持引流管通畅或经皮穿刺引流，需长时间药物治疗（生长抑素或生长抑素类似物），症状严重者需介入、手术等侵入性治疗，严重者可能导致死亡。

5）术后胆漏，胆肠吻合口瘘，需行腹腔通畅引流，部分胆痿可自愈，若常规治疗以及引流无效、病情恶化时，需行手术治疗。

6）术后手术部位或腹腔出血，可能需要行介入治疗，必要时再次手术。

7）术后腹腔积液，腹膜炎，腹腔感染，甚至腹腔脓肿，需再次手术可能。

8）术后胰瘘，若出现临床相关胰瘘，不排除二次穿刺甚至再次手术治疗，甚至危及患者生命。

9）术后肠粘连，粘连性肠梗阻。

10）营养性并发症：营养不良、体重减轻、贫血、腹泻和脂肪泻、代谢性骨病。

11）脑并发症：脑血管意外、癫痫。

12）呼吸并发症：肺不张、肺感染、胸腔积液、气胸等。

13）心脏并发症；心律失常、心肌梗死、心衰、心跳骤停。

14）血栓性静脉炎，以致肺栓塞、脑栓塞或其他部位栓塞。

15）多脏器功能衰竭（包括弥漫性血管内凝血）。

16）水电解质平衡紊乱。

17）诱发原有疾病恶化。

18）术中胃肠道损伤，导致术后胃肠漏，胃肠吻合口瘘可能。

19）术后胃排空障碍，出现术后腹胀、恶心、呕吐。

20）术后门静脉系统、肠系膜血管血栓形成。

21）胰性脑病。

22）术后成人呼吸窘迫综合症（ ARDS ）。

23）术后胰腺外分泌功能不全，导致血糖升高、甚至糖尿病可能。

24）术后胰腺内分泌功能不全，导致消化吸收功能障碍，导致顽固性腹泻等。

25）术后胰源性门静脉高压症，导致消化道大出血等。

26）术后胰源性胸水和腹水。

27）若为恶性肿瘤，肿瘤切除术后复发，远处转移。

28）术后胃肠道出血，应激性溃疡，严重者死亡。

29）如果卧床时间较长可能导致肺部感染，泌尿系统感染，褥疮，深静脉血栓及肺栓塞、脑栓塞等。

30）术后远期并发症：胆肠吻合术后可发生胆肠吻合口狭窄、胆管结石、胆管炎、肝脓肿；胃部分切除及胃肠吻合术后可能导致营养不良、吻合口溃疡、消化道出血、倾倒综合征；胰腺切除及胰肠吻合术后可能导致胰腺内分泌及外分泌功能不全、胰肠吻合口狭窄、慢性胰腺炎、胰管结石。

31）术后诊断可能与术中冰冻检查结果不一致，最终诊断根据术后病理结果决定。

32）其它目前无法预料的风险和并发症。

6. 研究过程中受试者出现上述不良事件时，将如何处理？

若发生不良事件应及时由医生或患者报告给研究者，研究者在病例报告表的相应位置做详细记录，研究者应在尊重患者意愿及选择的前提下协助患者积极处理不良事件，争取获得最佳的预后。同时对可能发生的不良事件进行预防。若发生严重不良事件时，研究者及医护人员将按照严重不良事件救治预案进行处理：报告：研究者向科室负责人及医院值班人员报告不良事件性质，并在 24 小时内报告伦理委员会及相关主管部门。及时救治受试者：一旦发生严重不良事件，根据受试者具体不良事件情况迅速采取相应诊疗措施，对受试者进行抢救，必要时送 ICU 诊治。记录：研究者在原始病案和 CRF 表中记录受试者的症状、体征、实验室检查，严重不良事件出现时间、持续时间、程度、处理措施和经过，保证记录完整、真实、准确、及时。填写严重不良事件报告表。随访：研究者对受试者不良事件进行随访，根据病情决定随访时间，在随访过程中给予必要的处理及治疗措施，确保将受试者损害降至最低，充分保证受试者安全。并且详细记录随访经过和处理结果。当发生严重不良事件时，研究将对受试者进行及时救治，并依据相关法律法规给予适当补偿。

7. 参加研究有哪些可能的好处？

参加本项研究，您的病情有可能获得改善，本项研究还有助于确定哪种治疗方法可以更安全有效地治疗与您具有相似病情的其他病人。

8. 参加研究需要支付有关费用吗？

研究员将应当公平、合理地选择受试者。除需要支付诊疗过程中产生的费用外，受试者参加本研究不支付其他任何费用。

9. 个人信息是保密的吗？

您的研究资料将保存在四川大学华西医院，研究者、研究主管部门、伦理审查委员会可查阅您的医疗记录。任何有关本项研究结果的公开报告将不会披露您的个人身份。我们将在法律允许的范围内，尽一切努力保护您个人医疗资料的隐私和个人信息。

10. 我必须参加研究吗？

参加本项研究是完全自愿的，您可以拒绝参加研究，或在试验的任何阶段随时退出本研究而不会受到歧视和报复，其医疗待遇与权益不受影响。如果您决定退出本研究，请与您的医生联系，以便妥善诊疗疾病。

受试者声明：我已经阅读了上述有关本研究的介绍，我的研究人员已向我充分解释和说明了本研究的目的、操作过程以及参加本研究可能存在的风险和潜在的获益，并回答了我所有相关问题。自愿参加本研究。

我同意☐ 或拒绝☐ 除本研究以外的其他研究利用我的研究资料和生物标本。

受试者正楷姓名：_____

受试者签名：_____ 日期：__ __ __ __ 年 __ __ 月 __ __ 日

受试者的联系电话：_____ 手机号：_____

法定代理人正楷姓名：_____ （如适用）

与受试者关系：_____

法定代理人签名：_____ 日期：__ __ __ __ 年 __ __ 月 __ __ 日

需法定代理人签署的原因：_____

见证人正楷姓名：_____ （如适用）

见证人签名：_____ 日期：__ __ __ __ 年 __ __ 月 __ __ 日

需见证人签署的原因：_____

医生声明：我已对上述参加本研究的自愿者说明了该项研究的有关细节，并且为他/她提供一份签署过的知情同意书的原件。我确认已向受试者详细解释了本研究的情况，特别是参加本研究可能产生的风险与受益、免费与补偿、损害与赔偿、自愿与保密等伦理原则和要求。

医生签名：_____ 日期：__ __ __ __ 年 __ __ 月 __ __ 日

医生的联系电话：_____

四川大学华西医院生物医学伦理审查委员会 联系电话：028-85422654，028-85423237