Official title: A Phase II Study to Evaluate the Feasibility and Safety of Hybrid Transvaginal Natural Orifice Transluminal Endoscopic Surgery for Treatment of Patients with Colon Cancer

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RESEARCH PARTICIPANT INFORMED CONSENT AND PRIVACY AUTHORIZATION FORM

Master Informed Consent Form

Protocol Title: **Feasibility and safety of hybrid transvaginal natural orifice transluminal endoscopic surgery for colon cancer: study protocol of a multicenter phase II trial (vNOTESCA)**

Approval No.: **WDRY2022-K053**

Sponsor By: **Department II of Gastrointestinal Surgery of the Renmin Hospital of Wuhan University**

Principal Investigator: **Dr. Tao Fu**
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You are being asked to take part in a research study. Participation in this study is voluntary. Even if you decide to join now, you can change your mind later.

We are carrying out a clinical study entitled "Feasibility and safety of hybrid transvaginal natural orifice transluminal endoscopic surgery for colon cancer", which has been reviewed and approved by the Clinical Research Ethics Committee of the Renmin Hospital of Wuhan University. The ethics committee has considered this research is compliant with the Hippocratic Oath and medical ethics. This study will be conducted in Renmin Hospital of Wuhan University, Beijing Friendship Hospital of Capital Medical University, Daping Hospital of Daping Hospital, the Second Affiliated Hospital of Zhejiang University, and the Third Xiangya Hospital of Central South University.

Before you decide whether to participate in this study, please read the following contents as carefully as possible. It will help you learn about the reason and duration of the research, and understand what you need to do and the possible benefits, risks and discomforts after participating in it. Your participation in this study is purely voluntary, which means you can either choose to participate or not.

You may discuss this study and the information contained in this document with someone close to you,

such as a partner, family member, friend, or doctor. The study doctor will explain this information sheet to you. If you are unsure about anything, the study doctor will answer any questions you may have.

After you have considered all the information relevant to this study and all your questions have been answered, if you agree to participate, you will be asked by the study doctor to sign and date the informed consent (at the end of this document) before proceeding with any study-related procedures.

1. Research Background:

Natural orifice transluminal endoscopic surgery (NOTES) is a technique that uses the natural orifice of the human body (such as the oral cavity, vagina, anus, etc.) to access the body cavity for biopsy and surgical operations. NOTES technology is known as the second revolution of minimally invasive surgery. Currently, the safest and most feasible natural cavity recognized internationally for NOTES surgery is the female vagina. hybrid transvaginal NOTES have been widely used for cholecystectomy and appendectomy, and their advantages in the surgical treatment of benign diseases have been confirmed by several prospective randomized controlled studies. At present, there are limited cases of hybrid transvaginal NOTES for colon cancer treatment and a lack of support from prospective randomized controlled studies. We are one of the earliest units in the world to perform hybrid transvaginal NOTES for colon cancer. More than 30 cases of hybrid transvaginal NOTES have been carried out by us, and rich experience has been accumulated. Our preliminary study showed that it is safe and feasible for hybrid transvaginal NOTES to be applied for colon cancer treatment. Compared with traditional laparoscopic and open surgery, Hybrid transvaginal NOTES show the advantages of less pain, faster recovery, and better cosmetic effect, and its radical effect is equivalent to them. However, due to the lack of large samples and long-term follow-up results, our conclusions need further validation.

2. Research Objective:

This study aims to further demonstrate the clinical efficacy of hybrid transvaginal NOTES in colon cancer, hoping to provide high-level evidence-based medical evidence for the application and promotion of this surgery in colon cancer, benefiting female patients with colon cancer greatly.

3. Inclusion and exclusion criteria:

Inclusion criteria: (1) Female; (2) Age: over 18 and below 80 years old; (3) BMI < 28 kg/m^2; (4) American Society of Anesthesiologists score of class I to III; (5) Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1; (6) Colonic adenocarcinoma by endoscopy with biopsy; (7) Tumor size ≤ 3 cm; (8) Involving a single colon segment: a. Right colon from the ileocecal valve up to and including the hepatic flexure. b. Left colon from the splenic flexure to the junction of the sigmoid and descending colon. c. Sigmoid colon between the descending colon and the rectum (at least 15 cm from the dentate); (9) Clinical stage cT1, T2, or T3, cN0, N1, N2; (10) No advanced local disease that renders laparoscopic resection impossible; (11) No transverse colon cancer (between distal hepatic flexure and proximal splenic flexure); (12) No distant metastasis in preoperative studies; (13) Complete preoperative colonoscopy demonstrating no synchronous colon cancers; (14) Require one of the following elective operations that may be safely performed by current techniques: a. Right hemicolectomy, b. Left hemicolectomy, c. Subtotal colectomy, d. Sigmoid colectomy; (15) Patients who agree with participating in the clinical study with informed consent. And with willingness and ability to comply with the requirements of the study protocol including follow-up.

Exclusion criteria: (1) Patients who have never experienced complete sexual intercourse before the operation; (2) Previous intestinal surgery with any cause; (3) cT4 tumor; (4) Complications of colon cancer (bleeding, obstruction, or perforation); (5) Previous neoadjuvant chemotherapy or radiotherapy for colon cancer; (6) Patients who are diagnosed with other malignancies within 5 years; (7) Vulnerable patients; (8) Vaginal stenosis; (9) Prior reconstructive surgery of the vagina not including hysterectomy; (10) Unstable angina or

participated in another clinical trial within 6 months; (14) Pregnancy or breastfeeding; (15) Any history of pelvic radiation; (16) Anticipated need for an ostomy at the time of operation; (17) Patients requiring urgent or emergent surgery; (18) Patients with a prior or suspected diagnosis of inflammatory bowel diseases such as Crohn's disease, ulcerative colitis, or familial polyposis.

4. What you need to do if participating in the study:

Before you are enrolled, you will undergo the following tests to determine whether you are eligible to participate in the study:

The doctor will ask about your medical history and give you a physical examination. You will be required to perform routine examinations such as electronic colonoscopy and chest and abdomen CT.

If you pass the above tests, the study will proceed as follows:

You will undergo hybrid transvaginal NOTES, and the follow-up will continue for more than 2 years after the standardized postoperative treatment. You should visit the hospital regularly to complete the questionnaire survey and reflect the changes in your condition to your doctor. Your doctor will follow up by phone, letter, door-to-door visit and collect your medical history and physical examination results.

Other matters needing your cooperation:

It is important that you visit the hospital at the follow-up time agreed between you and your doctor so that your doctor will be able to determine whether the treatment you have received is working. Gradually return to your normal diet and avoid overeating after surgery.

5. Benefits of participating in this research

The results of international literature studies and our preliminary small sample study show that hybrid transvaginal NOTES have the advantages of mild pain, rapid recovery, and good cosmetic results, and its radical effect is equivalent to traditional laparoscopic and open surgery. You and the community will probably benefit from this study. We hope that the information obtained from your participation in this study will help provide more information and develop new therapies for the future treatment of colon cancer. You will receive excellent medical care during the study.

6. Possible adverse reactions, risks, discomforts, and inconveniences of participating in this research

All surgical treatments may cause complications and even disease progression. If you have any discomfort during the study, any new changes in your condition, or any unforeseen circumstances, whether related to surgery or not, your doctor should be informed promptly, and he/she will make a judgment and medical treatment according to the situation. If an adverse event occurs during the clinical trial, experts in the medical committee will determine if it is related to the procedure.

You need to follow up on time in hospital or by telephone during the study, and sometimes have some physical and chemical tests, which may cause trouble or inconvenience.

7. Research costs, compensation, and damages

Cost of drugs and tests used in the study:

Surgery and follow-up examination are routine fee items, with no extra charges. You will not be reimbursed for additional costs incurred by participating in this study.

Compensation for participation in the study:
You will not receive any financial compensation for participating in this study.

Compensation for Damages:
If you suffer damage as a result of participating in the study, you may receive free treatment from the Renmin Hospital of Wuhan University and will be compensated according to the law.

8. Use of research results and confidentiality of personal information

When the study is completed, we will analyze the data. You will have the opportunity to know the results of the study through your doctor. You also can ask your doctor to explain them. The results of this study may also be published in journals or be reported at conferences, but they will not contain any information that may identify you.

To ensure privacy, records or samples published for research purposes will not attach your name and other identification information. At the same time, your information will be identified only by one code. Only the study physician and authorized personnel will be able to associate this code with your name through a list which will be kept securely at the study center.

If necessary, the applicant, the ethics review committee and the government management department can consult your information according to the regulations, in order to ensure whether the research is carried out normatively in the research center. They are bound by the confidentiality obligation and will not infringe on your privacy.

You have the right to control the use and disclosure of your personal information. You can ask to see your medical information whenever the law allows. You have the right to view all information collected about you through your doctor and ask for correction (if applicable).

9. Research-related new information

During the study, if there are changes in research procedures, new complications or major situations that may affect your health or willingness to participate, the research team will notify you. The researcher will notify you immediately and will discuss with you whether you want to continue to participate in this study. If you decide not to continue, the doctor will make a plan and your medical treatment and rights will not be affected. If you decide to stay in this study, the researcher may ask you to sign a new informed consent.

10. Your rights and responsibilities

Your rights
In the whole process of participating in the study, you are voluntary. If you decide not to participate in this study, it will not affect the other treatment you should receive. If you decide to participate in this study, you will be asked to sign this written informed consent. You have the right to withdraw from the trial at any stage without discrimination or unfair treatment, and your medical treatment and rights will not be affected.

Your responsibilities
Return to the hospital at the scheduled time for your visit

- Return to the hospital at the scheduled time for your visit
- If you want to terminate the study, you can tell your doctor at any time
- Be truthful about your medical history and current medical condition
- Follow the instructions of the researcher

- Tell your doctor about any discomfort you have noticed during the study.
- It is possible to cause risk to you or your fetus in any experimental treatment, so both you and your partner should avoid any activity that may result in pregnancy during the study. If you become pregnant during the study, please inform your doctor immediately.

11. What to do now:

It is up to you to decide whether to participate in this study or not. You can discuss it with your family or friends before your decision. Before you decide to participate in the study, please ask your doctor as many questions as possible until you fully understand the study. Thank you for reading the above material. If you decide to participate in this study, please tell your doctor and he/she will make all the arrangements regarding the study for you. Please keep this information with you.

12. Relevant contacts:

If you have any questions related to this study, please contact us by telephone: _____and _____researcher or related person). If you have any questions related to your rights/interests, or if you want to reflect on the difficulties, discontents, and concerns about your participation in this study. If you want to provide comments and suggestions related to this study, please contact the Ethics Committee for Clinical Research of the Renmin Hospital of Wuhan University, Tel: 027-88041911-81353.

SITE SPECIFIC CONSENT INFORMATION

Site Name: **Renmin Hospital of Wuhan University**

Study Title: **Feasibility and safety of hybrid transvaginal natural orifice transluminal endoscopic surgery for colon cancer: study protocol of a multicenter phase II trial (vNOTESCA)**

IRB Application Number: WDRY2022-K053

Principal Investigator: **Tao Fu**

Site Principal Investigator Contact Information:

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Subject statement:

I have been informed about the background, purpose, process, risks and benefits of this study. I was given sufficient time and opportunity to ask questions, and these questions were answered to my satisfaction.

I was told who to contact when I would like to reflect on difficulties, concerns, and problems, or provide further information and suggestions for research.

I understand that participation in the study is voluntary and I acknowledge that I have had sufficient time to consider and decided to voluntarily participate in this study. I have opportunities to consult with my physician for more information at any time, and I have the right to withdraw from the study at any time without any reason, without discrimination or reprisal, and without prejudice against my medical treatment or interests. In addition, the researchers did not force me to participate in the study using deception, inducement, and coercion.

I have known that my study doctor may decide to withdraw me from the study if my condition gets worse, if I have a serious adverse reaction, or if he/she feels that it is not in my best interest to continue to participate in the study. The sponsor or regulatory agency may also terminate the study during the duration without my consent. If this happens, my doctor will notify me promptly and discuss other options with me.

I have read this informed consent and agreed to participate in this study.

I will be provided with an original of the informed consent containing the signatures of me and the researcher and the date of signature.

Please sign and date your choice below:

YES □ _____ _____
Signature of Participant Date

_____
Telephone

NO □ _____ _____
Signature of Participant Date

_____
Telephone

YES □ **NO** □ _____ _____
Signature of Legal Representative Date

_____
Telephone

(Note: If the subject is incapacitated or has limited capacity, such as being included in a vulnerable group with mentally impaired/unconscious, the signature of the legal representative is required at the legal representative's signature)

_____ _____
Signature of Fair Witness Date

_____
Telephone

(Note: Only when subjects who have the normal informed ability but are unable to read the text (e.g., illiteracy and visual impairment) are included, a fair witness signature is needed. The researcher should retain the video material as evidence when the witness is informed)

Researcher Statement:

I have accurately informed the subject of this document and he/she has accurately read this informed consent. I certify that the subject has been allowed to ask questions and that he/she has given voluntary consent. I have given him/her a signed copy of the original informed consent.

Signature of Researcher	Date
Telephone	