Study Protocol

Two-finger digital rectal examination for the diagnosis of anal fistula: protocol for a randomized controlled trial

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Background: Anal fistula is an anorectal infectious disease caused by a perianal abscess or perianal disease. Accurate anorectal examinations are of great significance. The two-finger digital rectal examination (TF-DRE) has been used in clinical practice, with a lack of comprehensive research on the value of the TF-DRE in the diagnosis of anal fistula. This study will compare the difference in the diagnostic value of the TF-DRE, traditional digital rectal examination (DRE), and anorectal ultrasonography in the diagnosis of anal fistula.

Methods: For patients who meet the inclusion criteria, a TF-DRE will be performed to explore the number and location of the external and internal orifices, the number of fistulas, and the relationship between the fistula and the perianal sphincter. A DRE and anorectal ultrasonography will also be performed, and the same data will be recorded. To make a comparison, the final diagnosis results of the clinicians during the operation will be taken as the gold standard, the accuracy of the TF-DRE in diagnosing anal fistula will be calculated, and the significance of the TF-DRE in the preoperative diagnosis of anal fistula will be studied and analyzed. All the statistical results will be analyzed using SPSS22.0 (IBM, USA), and a P value <0.05 will be considered statistically significant.

Discussion: The research protocol details the advantages of the TF-DRE compared to the DRE and anorectal ultrasonography in the diagnosis of anal fistula. This study will provide clinical evidence of the diagnostic value of the TF-DRE in the diagnosis of anal fistula. Currently, there is a lack of high-quality research using scientific methods on this innovative anorectal examination method. This study will provide rigorously designed clinical evidence on the TF-DRE.

Registration: Chinese Clinical Trials Registry ChiCTR2100045450.

Keywords: Two-finger digital rectal examination (TE-DRE); digital rectal examination (DRE); ultrasonography; anal diseases; accuracy

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Introduction

Anal fistula is an anorectal infectious disease caused by perianal abscess or perianal disease. Its incidence is second only to hemorrhoids, accounting for 1.67–3.6% of all anorectal diseases (1,2), with a male to female ratio of 1.8:1.0 (3,4). The disease causes great physical discomfort, significantly effects patients' normal daily quality of life, and places a great psychological burden on patients (5). Surgery is the mainstay of treatment for anal fistulas, but the recurrence rate is as high as 10% after surgery, especially for complex anal fistulas, and post-operative sequelae including anal incontinence and mucosal eversion are common (6-10). Additionally, highly complex anal fistulas can lead to perianal infection (11). This infection can spread along the muscle planes and invade the pelvis, causing serious complications including rectovaginal fistula, rectourethral fistula, and rectovesical fistula, and cause mortality due to infection, sepsis, and cancer (2,12-14).

There are two main reasons for the post-operative recurrence of anal fistula. The first is a lack of clear diagnosis and confirmation of the lesion shape before the operation, and the second is that the internal orifice and deep fistula are not effectively treated during surgery (15,16). Thus, very specific requirements for the preoperative diagnosis of anal fistula are needed. Before the operation, it is necessary to fully understand the number, depth, direction, scope, and position of the internal opening to ensure that the damage to the anal sphincter is minimized during the operation, protect the function of the sphincter muscle, reduce the occurrence of complications, and improve the success rate of one operation.

Anorectal examinations can greatly reduce the missed diagnosis rate of anal fistulae, and the misdiagnosis of anal fistulae with no clear external orifices (17). The two-finger digital rectal examination (TF-DRE) is an examination method improved by Professor Zheng Lihua based on the traditional digital rectal examination (DRE). It has been used for nearly ten years and extensive clinical evidence on the DRE has been gathered. Clinical practice suggests that this method significantly reduces missed diagnosis as well as misdiagnosis, while characterizing the anal fistula in more detail. Yet, there is a lack of comprehensive research on the value of the TF-DRE in the diagnosis of anal fistula. The purpose of this study is to provide scientific evidence on the TF-DRE.

To date, research on the diagnosis of anal fistula has mainly focused on imaging examination methods, such as computed tomography (CT), magnetic resonance imaging (MRI), and ultrasonography (18-21). MRI accurately demonstrates the anatomical relationship between the lesions and surrounding tissues, and provides important imaging evidence for diagnosis and surgical treatment (22-24). Currently, there are three ultrasound examination methods for anal fistulas, transperineal ultrasonography, transrectal ultrasonography, and endoscopic ultrasonography, all of which have high rates of fistula misdiagnosis (25-27).

Other traditional examination methods include the routine inspection examination, DRE, anoscopy, probe examination, and fistula staining. The DRE provides a relatively accurate diagnosis of subcutaneous or submucosal fistulas and sinuses, but the feel of a fistula is similar to the tactile sensation of healed scar tissue, and thus it is sometimes difficult to distinguish between scar tissue and fistulas (28). The diagnosis rate for highly complex anal fistulas is extremely low. The methylene blue test injects methylene blue solution into the fistula through the external orifice to determine the position of the internal orifice, but the effect is suboptimal when the tissue around the internal orifice and the fistula are not smooth (29,30).

Through this diagnostic, prospective, controlled study, we will evaluate the difference in the diagnostic value of the TF-DRE, DRE, and anorectal ultrasonography in the diagnosis of anal fistula. Taking the surgical results as the gold standard, we will examine this simple and efficient new method for the diagnosis of anal fistula, and further improve the diagnosis of anal fistula. We hope to provide clinical evidence of the diagnostic value of the TF-DRE in the diagnosis of anal fistula based on our findings. We present this article in accordance with the SPIRIT reporting

Highlight box

Key findings

- We have established a new physical examination method for anal fistula.

What is known and what is new?

- A traditional digital rectal examination and anorectal ultrasonography are often used in the diagnosis of anal fistula.
- This study describes an accurate and convenient method for examining the condition of anal fistula.

What is the implication, and what should change now?

- A comprehensive examination will help surgeons to successfully treat anal fistulas, especially in complex cases.

Table 1 Timetable of study

Tasks	Study stage			
	Enrollment	Assignment	Complete	
			Pre-operation	Intra-operation
Timepoint	–2	–2	–1	0
Enrollment				
Eligibility	•			
Informed consent	•			
Assignment		•		
DRE	•	•	•	•
Anus ultrasonography	•	•	•	
Anus pressure detection	•	•	•	
TF-DRE	•	•	•	•
Adverse events	•	•	•	•

• indicates the item was done at a certain time point. DRE, digital rectal examination; TF-DRE, two-finger digital rectal examination.

checklist (available at https://jgo.amegroups.com/article/view/10.21037/jgo-23-402/rc).

Methods

Study design

This study will be a diagnostic, prospective, controlled study. This study has been registered with the Chinese Clinical Trials Registry (https://www.chictr.org.cnl; protocol version: 2021-12-10 1.0).

Research settings

This study will include patients diagnosed with anal fistulas and hospitalized for surgical treatment at the Department of Proctology, China-Japan Friendship Hospital (Beijing, China). This study will be conducted under the supervision and monitoring of the Ethical Committee of the China-Japan Friendship Hospital. Timepoint is shown in *Table 1*.

Study population and recruitment

All patients with a diagnosis of anal fistula ages ≥18 years, will be eligible for inclusion in the study. This study will use the guidelines for the treatment of perianal abscesses and anal fistulas formulated by the American College of Colorectal Surgeons in 2016 (31) as the diagnostic criteria for anal fistula. To be eligible for inclusion in this study, patients will have to meet the following inclusion criteria: (I) ages 18 to 70 years; (II) meet the diagnostic criteria for an anal fistula; (III) agree to undergo anal fistula surgery; and (IV) agree to voluntarily participate in the clinical research, sign the informed consent form, and be able to cooperate with the clinical follow-up. Patients will be excluded from the study if they meet any of the following exclusion criteria (I) have coagulation dysfunction; (II) have a rheumatic disease; (III) have severe liver and kidney insufficiency; (IV) have uncontrolled blood pressure; (V) have a mental disorder, or find it difficult to cooperate with the research; (VI) are pregnant or breast feeding; and/or (VII) have an inflammatory bowel disease, diabetes, tuberculosis, acquired immunodeficiency syndrome, or an anorectal malignant tumor.

To recruit subjects for this study, subject recruitment information will be published on the Internet and advertised in outpatient clinics. The subjects will be enrolled after being screened as per the formal treatment process and admission criteria. Before enrollment, the patients will be informed that the surgeon will use an effective method during the treatment process. To minimize the bias of the trial, after the clinical follow-up is completed, the data will be sent to a third party for statistical analysis. Finally, the physicians and statisticians will jointly announce the statistical results.

Randomization

The random number table method will be used to divide the patients into two groups. The first group of patients

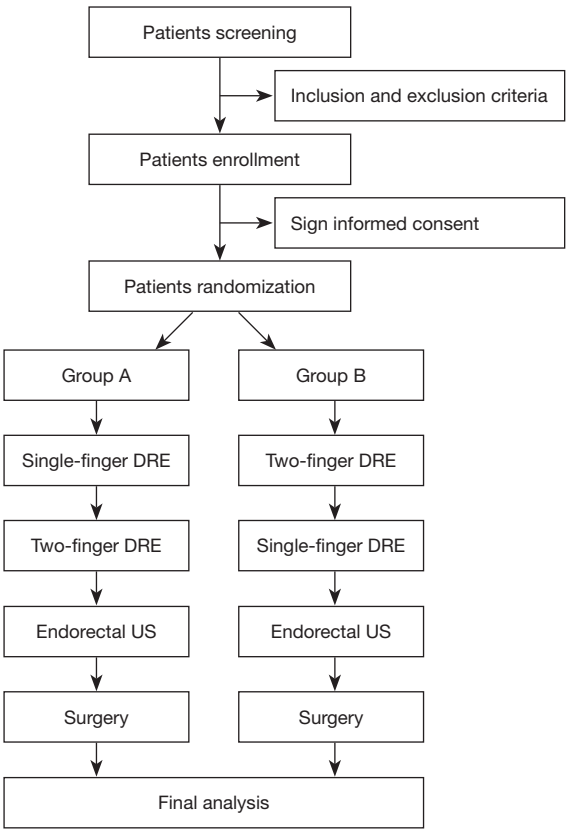

Figure 1 Study flowchart. DRE, digital rectal examination; US, ultrasound.

will receive the traditional DRE by the first doctor, and the second doctor will perform the TF-DRE. The second group of patients will also be examined by the first doctor. The doctor will perform the TF-DRE, and a second doctor will perform the traditional DRE. All the patients will undergo an anorectal ultrasonography by a sonographer.

Blind

The anal physical examination will be completed and recorded by two doctors independently, and the results will be sealed and handed to a third person. The two doctors will be unaware of each other's examination results for the same patient. The sonographer will be blinded to the results of the physical examination.

Endpoints and study parameters

Primary endpoint

The primary endpoint is the accuracy of the diagnosis of anal fistula.

Study parameters

The study parameters include the clinical information, laboratory test results, imaging information, postoperative complications, 28-day mortality after surgery, repeated surgery, length of hospital and intensive care unit stay, and repeated hospitalization.

Ethics and informed consent

This study will be conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study protocol has been approved by the Ethical Committee of the China-Japan Friendship Hospital (No. 2022-NHLHCRF-LX-02-0121). Informed consent will be obtained from the patients when they are enrolled. Participation in the study does not represent a risk greater than or different from the general surgical treatment of patients with an indication for colorectal surgery, since patients would have two DREs (that might bring some discomfort). There is no economic burden for participation in this study. It is possible that patients will benefit from participating in the study, as the regular and standard physical examinations will also be conducted.

Procedure for obtaining informed consent: The researcher will provide the subject or their legal representative with an understandable and ethical committee-approved informed consent form and give the subject or their legal representative sufficient time to consider the form. The subjects will not be enrolled in the study until a signed written informed consent form has been obtained. During subject participation, the subjects will be provided with any updated versions of the informed consent form along with other written information. As an important document of the clinical trial, the informed consent form will be kept for future reference. The results of the research related to this study may be published in medical journals, but patient's information will be kept confidential as required by law, and the patients' personal information will not be disclosed unless required by law. The hospital's ethics committee may consult the patients' information as required.

Diagnostic examinations

The following process will be adopted for all the patients (*Figure 1*):

(I) All the clinical information in the case record forms (CRFs) will be recorded;

(II) The patients will undergo a postoperative examination to observe:

- ❖ Any changes in their symptoms, incisions, and vital signs;
- ❖ Their laboratory test results; and
- ❖ Their radiological imaging results.

After the surgery, we will check and evaluate the patients daily until discharge or until the event endpoint (i.e., anastomotic leakage) is reached. Anastomotic leakage will be assessed using a visual analogue scale score of zero to ten. The patients will receive repeated laboratory tests or imaging examinations as necessary. The gold standard in the diagnosis of anastomotic leakage is the presence of a dehiscent anastomosis at relaparotomy/relaparoscopy or the efflux of feces from a percutaneous drain.

Clinical parameters

The following clinical information will be recorded in the CRFs: clinical and mental status, vital signs, including respiratory rate, heart rate, blood pressure, temperature, and urine and stool status. The laboratory results will include routine blood, C-reactive protein, serum level of creatinine, urea, and electrolyte tests.

Additional radiological imaging tools will only be used as necessary. This decision will be made by the treating surgeon or surgical resident. If an abdominal CT scan is considered necessary, the standardized radiological CT parameters will be recorded on the CRFs.

Procedures

Our research will be divided into the following two stages: (I) the screening stage; and (II) the intraoperative exploration stage. In the first stage, the main task will be to enroll patients in the study according to the inclusion and exclusion criteria and obtain their signed informed consent. Before being enrolled in the study, the doctors will get the patients' medical history, and conduct preoperative examinations, including the DRE, intrarectal ultrasonography, and other screening examinations.

Preoperative examination

The patient will be instructed to lie on the examination bed in the right arched position, flex their hip to 90°, and expose their anus. First, an anus inspection will be performed, the number and location of the external orifice of the anal fistula will be recorded, and details of the digital anus examination and operation steps will be briefly explained to the examinee. After which, the following procedures will be conducted:

DRE

The doctor will wear a glove on their right hand, and apply an appropriate amount of lubricant, such as paraffin oil, Vaseline, and soap. First, the doctor will place their index finger on the outside of the anus and gently massage the anus, instructing the patient to relax and breathe deeply to relax the anal sphincter. The doctor will then slowly press the tip of their index finger into the anus and rectum and check the anus in a 360° clockwise direction. The doctor will carefully touch and press the anus, anal canal, and rectum to explore and record the number and location of the external orifice and internal orifice of each anal fistula, the number of fistulas, and record the relationship between each fistula and the perianal sphincter (*Figure 2*). After the index finger has been withdrawn, the doctor will observe and identify any secretions and attachments, such as mucus, pus, or blood, on the fingertip, and record the color and character.

TF-DRE

The doctor will wear a glove on their right hand and apply an appropriate amount of lubricant, such as paraffin oil, Vaseline, or soap. First, the doctor will place their index finger on the outside of the anus and gently massage the anus, instructing the patient to relax and breathe deeply to relax the anus sphincter. After the sphincter is relaxed, the doctor will slowly press the tip of their index finger into the anus and rectum. At the same time, the doctor will place the thumb of their right hand on the skin outside the anus corresponding to the index finger. The doctor will press and touch the thumb to the index finger, bend the index finger, and make a pinching action with the two fingers, so that the thumb is in contact with the anus. For the 360° clockwise examination, the doctor will use their index finger to carefully touch and press the anus, anal canal, and rectum, explore and record the number and location of the external orifice and internal orifice of each anal fistula, the number of fistulas, and their relationship with the perianal sphincter. After the index finger has been withdrawn, the doctor will observe and identify any secretions and attachments, such as mucus, pus, or blood, on the finger cuff, and record the color and character.

After DRE, patients will undergo intrarectal ultrasonography.

In the second intraoperative exploration stage, the

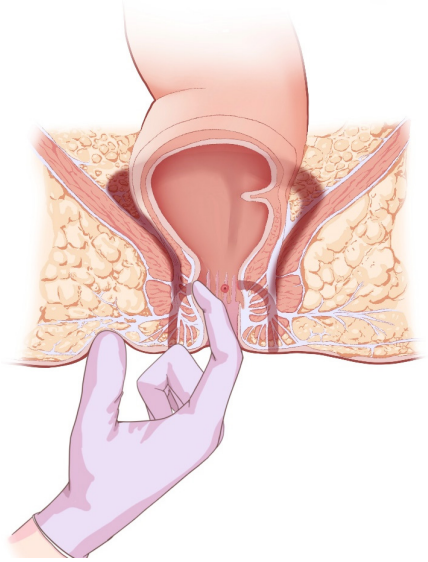

Figure 2 The doctor will wear a glove on their right hand with lubricant. First, gently massage the anus to relax the anus sphincter. then slowly press the tip of index finger into the anus and rectum. At the same time, place the thumb on the skin outside the anus corresponding to the index finger. The doctor will press and touch the thumb to the index finger, bend the index finger, and make a pinching action with the 2 fingers, so that the thumb is in contact with the anus. For the 360° clockwise examination, the doctor will use their index finger to carefully touch and press the anus, anal canal, and rectum, explore and record the number and location of the external orifice and internal orifice of each anal fistula, the number of fistulas, and their relationship with the perianal sphincter.

patient will be instructed to lie on the operation bed in the right arched position, with their hip flexed to 90°, and their anus exposed. After administering the general intravenous anesthesia, the surgeon will conduct an intraoperative exploration to record the number and location of the external orifice and internal orifice of each anal fistula, the number of fistulas, and their relationship with the perianal sphincter (*Figure 1*).

Outcomes

The outcomes include the number and positions of the external and internal orifices, the number of fistulas, and their relationship with the perianal sphincter of the anal fistula, which will be recorded by the DRE, TF-DRE, intra-anorectal ultrasound, and anal fistula surgery. The position of the internal and external orifices will be recorded using the bladder lithotomy position, and the relationship between the fistula and the perianal sphincter will be recorded using the Parks classification method.

Adverse event records

We will document any adverse events that occur during the clinical trial. An adverse medical event that occurs after a patient or clinical trial subject receives a drug or intervention, but is not necessarily causally related to the treatment, is called an adverse event. Serious adverse events are defined as events that require hospitalization, prolong hospitalization, cause disability, affect work ability, endanger life, cause death, and cause congenital deformities during clinical trials. Clinical adverse events may occur during the subject's treatment. If an adverse event (including a major adverse event) occurs, the occurrence time, clinical manifestations, treatment process and duration, outcomes, and the related events of the adverse events will be recorded in detail on the case report form. If there are abnormal laboratory tests, the patients will be followed up until the test results return to normal, or to the level before the intervention, or until it is determined that the test results are not related to the research operation. Serious adverse events will be recorded in a serious adverse event form and reported to the Ethics Committee within 24 h.

Data collection

All the data will be recorded in and extracted from an electronical medical records system. The following data will be collected: demographic information, baseline characteristics, surgery information, and outcome information. All the extracted data will be put in Excel spreadsheet (Microsoft, USA) for the statistical analysis.

Statistical analysis

Sample

This study is a diagnostic, prospective, controlled study. The accuracy rate of anal fistula diagnosis reported in the literature is about 90% (25,26,29,31), and the accuracy rate of the TF-DRE is 99% according to our experience. We used an accuracy rate of 90% when calculating the sample size.

N is the sample size. In the sample size estimation, we considered the following elements: (I) the level of the

authenticity index (i.e., the sensitivity, and specificity); (II) the test level (α=0.05); that is, the probability of a type I error; and (III) the allowable error (δ=0.10). The sample size calculated by SPSS22.0 (IBM, USA) statistical software was 130 cases.

Statistics

The statistical analysis will be performed using the SPSS 22.0 (IBM, USA) statistical software package. All statistical tests will be two-sided, and a P value <0.05 will be considered statistically significant for the differences tested. We will statistically calculate and compare the diagnostic accuracy of the various indicators recorded by the digital rectal examination, TF-DRE, and anorectal intracavitary ultrasound, using Chi-square test. The diagnosis accuracy rate will be calculated as follows: diagnosis accuracy rate = the number of cases with accurate diagnosis / total number of cases × 100%. Accurate diagnosis is confirmed by the results of surgery.

Privacy

The DRE and anorectal extraction will be performed at the Department of Proctology, China-Japan Friendship Hospital. If the patient is of the opposite sex, a medical and health practitioner will be required to attend the examination. The anorectal ultrasonography will be performed by attending physicians from the Department of Ultrasound Diagnosis of the China-Japan Friendship Hospital, and the anal fistula operation will be performed by experienced physicians from the Department of Proctology, China-Japan Friendship Hospital.

Discussion

The recurrence of anal fistulas is closely related to the lack of a clear diagnosis before surgery. Accurate anorectal examinations are very important if the recurrence rate of anal fistulas is to be reduced. In this study, we will use the surgical findings as the gold standard to evaluate differences in the diagnostic value of the TF-DRE, DRE, and intrarectal ultrasonography in the diagnosis of anal fistula, to explore the advantages of anorectal extraction in the diagnosis of anal fistula, and further improve the accuracy of anal fistula diagnosis. As an innovative method, extensive evidence on the TF-DRE has been accumulated based on its early clinical application, but there is still a lack of high-quality research using scientific methods in the current literature. This study will provide rigorously designed clinical evidence for the TF-DRE. We hope that these results will provide clinical evidence of the diagnostic value of the TF-DRE in the diagnosis of anal fistula, and thus help clinicians to improve the surgical success rate of anal fistulas, especially highly complex anal fistulas, and ultimately reduce the pain of patients. However, as the results of surgery is considered golden standard of anal fistula, the success of surgery partly depends on surgeon's experience. We will ensure the success by careful operation conducted by experienced doctor and intra-operation ultrasonography.

Writing process

The writing of this article was based on the recommendations for the publication of clinical trial protocols and related documents in the SPIRIT 2013 statement in the "Journal of Evidence-Based Medicine in Traditional Chinese Medicine" and the recommendations for the research design and clinical application of diagnostic test accuracy in the "Concord Medical Journal".

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Footnote

Reporting Checklist: The authors have completed the SPIRIT reporting checklist. Available at https://jgo.amegroups.com/article/view/10.21037/jgo-23-402/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jgo.amegroups.com/article/view/10.21037/jgo-23-402/coif). RDP reports payment from Servier, Bayer, Merck and AstraZeneca; support for attending ASCO and ESMO from Roche and Ipsen, fee for lectures from AstraZeneca, BMS, Servier, Bayer, Astellas and Pfizer. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are

appropriately investigated and resolved. This study will be conducted in compliance with the Declaration of Helsinki (as revised in 2013). The study protocol has been approved by the Ethical Committee of the China-Japan Friendship Hospital (No. 2022-NHLHCRF-LX-02-0121). Informed consent will be obtained from the patients when they are enrolled.

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