A Prospective, Randomized Controlled Study Comparing the Integrated Posterior–Anterior–Lateral (PAL) Approach and the Posterior Approach in Robot-Assisted Radical Prostatectomy

Research Protocol

Research Unit: The First Affiliated Hospital of Zhengzhou University

Principal Investigator: Xuepei Zhang

Contact Number: 13837110911

NCT ID: Not yet assigned

May 15, 2024

I. Research Background

Radical prostatectomy is the standard treatment for localized prostate cancer. Rassweiler et al. first reported robot-assisted radical prostatectomy (RARP) in 2001. Given the Da Vinci robot's high-definition three-dimensional imaging technology and flexible yet stable robotic arms, it is particularly suited for performing more precise dissection, anatomy, and suturing within confined spaces. Consequently, RARP has rapidly gained popularity worldwide and has even replaced traditional laparoscopic and open surgery in some hospitals. Patel et al. proposed the "pentafecta" for radical prostatectomy: long-term cancer control, urinary continence preservation, erectile function preservation, absence of surgical complications, and negative surgical margins. This remains the goal pursued by urologists. To achieve better treatment outcomes for patients, surgeons domestically and internationally have conducted in-depth research on various RARP approaches, such as the anterior approach, posterior approach lateral approach, and transvesical approach. However, each RARP approach has its own advantages and disadvantages. To maximize the benefits of each approach, based on our center's experience with over 1000 radical prostatectomies, we were the first in China to propose the PAL combined approach RARP in 2022. This approach involves initially using the posterior approach to separate the vas deferens, seminal vesicles, and Denonvilliers' fascia, followed by the anterior

approach to separate the retropubic space, and then the lateral approach to separate the bladder neck and preserve the neurovascular bundles (NVB) as much as possible.

II. Study Objectives

(1) Study Objective

This study aims to compare the perioperative outcomes, pathological results, and early functional outcomes of the PAL combined approach RARP and the posterior approach (Retzius-sparing) RARP in the treatment of prostate cancer.

(2) Study Significance

1. To provide a new, safe, and effective surgical approach (not a non-surgical method) for robotic radical prostatectomy in clinical practice.
2. To provide a better foundation for the application of the PAL combined approach RARP.

III. Research Trial Management

The center will appoint one Principal Investigator overall, one Co-Investigator, and one Lead Statistician. Standardized statistical analysis methods will be applied. The trial will be conducted strictly in accordance with the protocol, ensuring the timely, accurate, and truthful completion

of case report forms. Researchers will receive training prior to the trial's initiation to familiarize themselves with the study protocol and unify assessment criteria.

Laboratory test reports must contain all essential items, including the date, test items, test results, and their normal reference ranges. A strict serious adverse event reporting system will be established.

If you have any questions regarding this study, you may contact the Principal Investigator.

Name	**Role in Study**	**Phone Number**
Xuepei Zhang	Principal Investigator	13837110911
Jinshan Cui	Investigator	13243131252
Jin Tao	Investigator	-
Yunlong Liu	Investigator	-
Zhenhao LI	Investigator	-

IV. Rationale for the Trial

1. Surgeons domestically and internationally have conducted in-depth research on various RARP approaches, such as the anterior, posterior, lateral, and transvesical approaches. However, each RARP approach has its own advantages and disadvantages.
2. Our center was the first in China to propose the PAL combined approach RARP in 2022. This approach involves initially using the posterior approach to separate the vas deferens, seminal vesicles, and Denonvilliers' fascia, followed by the anterior approach to separate the retropubic space, and then the lateral approach to separate the bladder neck and preserve the neurovascular bundles (NVB) as much as

possible. There are currently no prospective studies comparing this combined approach with other approaches.

V. Subject Selection and Withdrawal

(1) Inclusion Criteria:

Age ≥ 40 years and ≤ 80 years;

Patients diagnosed with prostate cancer by prostate biopsy;

Clinical T stage ≤ T3a;

Full understanding of the clinical trial protocol and provision of signed informed consent.

Any outpatient or inpatient volunteer patient who meets all the above criteria can be enrolled as a subject.

(2) Exclusion Criteria:

Pre-existing urinary incontinence;

Previous endoscopic prostate surgery;

Presence of severe underlying diseases rendering the patient unable to tolerate surgery or with a life expectancy of < 5 years;

Presence of metastatic disease or suspected lymph node involvement at diagnosis;

Patients deemed by the investigator as unsuitable for participation in this clinical trial.

Any patient meeting any of the above criteria cannot be enrolled as a subject.

(3) Discontinuation (Withdrawal) Criteria:

This refers to all patients who have signed the informed consent form, passed screening, and entered the trial but subsequently withdraw from the clinical trial.

Common reason: The patient requests to stop the trial.

When a patient discontinues, the investigator must record the reason for discontinuation in the case report form and complete all possible assessments and examinations, documenting the last condition, including the last trial-related procedures performed. For discontinuations due to adverse events, this must be recorded in the case report form, and the sponsor must be notified. Discontinued cases will be included in the analysis according to different scenarios.

VI. Study Protocol

Study Design

This is a prospective, randomized controlled, single-center clinical study. It primarily aims to compare the perioperative outcomes, pathological results, and early functional outcomes of PAL combined approach RARP and posterior approach (Retzius-sparing) RARP in the treatment of prostate cancer. All patients meeting the inclusion/exclusion criteria will be randomly assigned to one of two groups: the PAL combined approach group or the posterior approach group. This study plans to enroll no fewer than 30 patients per group.

Inclusion Criteria

Detailed inclusion and exclusion criteria are listed above. The key inclusion criterion is patients diagnosed with prostate cancer by biopsy and scheduled to undergo robot-assisted radical prostatectomy.

Randomization

Eligible subjects will be randomized in a 1:1 ratio to either the PAL combined approach group or the posterior approach group. The randomization process will be performed by an independent, dedicated statistician.

Surgical Methods

All patients will undergo surgery according to the standard procedures for robot-assisted radical prostatectomy.

Posterior Approach (Retzius-sparing) RARP: Adhesions of the sigmoid colon are first released to expose the pouch of Douglas. The peritoneum is incised at the rectovesical pouch, taking care not to damage the ureters. The bilateral vas deferens are carefully dissected. Following the bilateral vas deferens leads to the identification and dissection of the bilateral seminal vesicles. The small arteries of the seminal vesicles can be managed using Hem-O-lok clips before cold knife transection, or using bipolar coagulation before transection. The bilateral seminal vesicles are freed. Denonvilliers' fascia is incised, and blunt dissection is performed along the anterior rectal fat plane towards the prostate apex. The parietal peritoneum of the rectovesical reflection is incised. The seminal vesicles and vas deferens are dissected and transected. Denonvilliers' fascia is incised transversely. Blunt dissection is performed along the posterior plane of the prostate towards the apex. The bladder neck is dissected and incised. Blunt dissection is performed intrafascially towards the apex. The puboprostatic ligaments and posterior urethra are dissected and transected, and the prostate is completely removed.

PAL Combined Approach RARP: Posterior Access The sigmoid colon was mobilized, and dissection proceeded along the posterior bladder wall to expose the pouch of Douglas. The rectovesical peritoneal reflection was incised to identify and preserve the bilateral ureters, vas deferens, and seminal vesicles. Dissection was performed dorsal to the seminal vesicles to identify and open Denonvilliers' fascia. The fascia was then dissected along the posterior plane of the prostate until reaching the prostatic apex, with careful attention to avoiding rectal injury. The vas deferens was subsequently transected, and the seminal vesicles were dissected. A triangular anatomical zone was developed

between the bladder neck, prostate base, and right neurovascular bundle to facilitate subsequent dissection steps. **Anterior Access** The preperitoneal space was developed by dividing the medial umbilical ligaments and the urachus, gaining access to the retropubic space (Fig. 1D). At this stage, the dorsal vascular complex was left intact. The endopelvic fascia, puboprostatic ligaments, and other anterior supporting structures were preserved to maintain anatomical integrity. **Lateral Access** The dissection plane along the bladder neck was defined. Building on the previously developed posterior plane, the triangular space bordered by the bladder, prostate base, and neurovascular bundle was further expanded. The mobilized seminal vesicles were retracted through this corridor to provide controlled traction. The bladder neck was then sharply divided close to the prostate, releasing any residual attachments and preserving surrounding muscle and connective tissue. The prostatic pedicles were subsequently clipped and dissected under direct vision to maintain hemostasis and anatomical precision. **Neurovascular Bundle Dissection** With the right seminal vesicle retracted toward the midline, a working plane was developed between the prostatic capsule and surrounding fascia. Dissection proceeded in an antegrade manner to release the neurovascular bundle without the use of thermal energy. The same approach was applied to the contralateral side to ensure bilateral nerve preservation. **Apical Dissection and Urethral Division** The prostate was elevated cephalad to expose the apex and adjacent posterior structures. Dissection at the apical region was performed with careful attention to preserving the maximal length of the urethral stump. Blunt and sharp dissection was carried out beneath the dorsal venous complex to avoid injury to anterior vascular structures. The pelvic fascia and puboprostatic ligaments were preserved. The urethra was then incised posteriorly under direct vision, completing the apical dissection and

allowing for en bloc removal of the prostate. After prostate dissection, continuous urethrovesical anastomosis was performed using a 3-0 suture.

VII. Observation Indicators

Primary Observation Indicator:

The primary observation indicator is the urinary continence rate after catheter removal. The urinary continence rate is defined as the number of patients with recovered continence per group divided by the total number of patients in that group. Urinary continence rates will be assessed at 1 day, 1 week, 3 months, 6 months, and 1 year after catheter removal. Recovery of urinary continence is defined as not using any pads or using only 1 safety pad per day with no leakage. Urinary incontinence is defined as using more than 1 pad per day. Immediate continence and early continence are defined as recovery of continence within 7 days and within 3 months after catheter removal, respectively.

Secondary Observation Indicators:

(1) Perioperative indicators, such as: operative time, estimated blood loss, intraoperative and postoperative complications, time to drain removal, postoperative hospital stay;

(2) Positive surgical margin status in the pathology report.

VIII. Ethical Requirements and Patient Informed Consent

This clinical trial will be conducted in accordance with the Declaration of

Helsinki (1996 version) and relevant Chinese regulations and guidelines for clinical trial research. The trial protocol must be approved by the Ethics Committee of each participating institution before the trial commences.

Before each patient is enrolled in this trial, the investigating physician is responsible for providing a complete and comprehensive explanation, in written form, to the patient or their designated representative, regarding the trial's purpose, procedures, and potential risks. Patients should be informed that they have the right to withdraw from the trial at any time. Each patient must be given a copy of the informed consent form before enrollment. The investigating physician is responsible for ensuring that each patient signs the informed consent form before entering the trial and for retaining the form in the study files.

IX. Statistical Analysis

Statistical tests will employ parametric methods or models wherever possible. All statistical tests for indicators will be two-sided, and a P-value $\leqslant$ 0.05 will be considered statistically significant.

Descriptive statistics for quantitative indicators will include the mean, standard deviation, median, and interquartile range. Descriptive statistics for categorical indicators will include counts and percentages. Statistical analysis will be performed using professional software such as SPSS, SAS, and R.

X. Data Retention

The investigator shall retain all study documents, including identification of all participating subjects (enabling effective cross-referencing of different records, such as hospital source records), all original signed informed consent forms, and all case report forms, etc. The investigator shall retain the clinical trial data for 5 years after the completion of the clinical trial.

XI. Expected Timeline for the Clinical Trial

(1) Trial preparation period: Month 1.

(2) Clinical trial observation period: Months 2 – 8.

(3) Data collection, statistical analysis, and summarization period: Months 8 -18.