Informed Consent Form

Clinical trials on the safety and effectiveness of neoadjuvant stereotactic radiotherapy combined with surgical treatment for patients with renal cell carcinoma with inferior vena cava tumor thrombus

You are invited to participate in this study because you meet the following Inclusion criteria:

(1) Age ≥ 18 years old.

(2) Imaging examination of renal cell carcinoma with inferior vena cava tumor thrombus.

(3) Inferior vena cava tumor thrombus graded from Mayo II to Mayo IV.

(4) Oncologists believe that patients are suitable for preoperative stereotactic ablative body radiotherapy (SABR) to treat inferior vena cava tumor thrombus.

(5) Urologists believe that patients are suitable for radical nephrectomy and inferior vena cava thrombectomy to treat renal cancer and inferior vena cava tumor thrombus.

(6) ECOG 0-2.

(7) Able to complete enhanced CT or enhanced MRI (either one) examination.

(8) Able to sign this Informed Consent Form.

Your research doctor or research staff will fully explain the contents of the informed consent form for you. Please carefully read this informed consent form and make a cautious decision whether to participate in the study. If you are participating in another research, please inform your research doctor or research staff.

The content / nature, risks and other important information of this study are as follows:

Director Ma Lulin will carry out this study.

I. Why to conduct this research?

(I) The background of this study is as follows:

Stereotactic radiotherapy (SBRT) or stereotactic ablation radiotherapy (SABR) refers to precise and concentrated radiotherapy for lesions outside the brain, which is given in small fractions (single dose belongs to the ablation dose range). With the progress of technology and the accumulation of experience, stereotactic radiotherapy technology has become more and more sophisticated and rapid. In recent years, a systematic review of 10 studies involving 126 patients with primary renal cell carcinoma who lost the chance of surgery shows that the weighted local control rate is 92.9% and the weighted severe toxicity is 3.8%. Recent prospective studies continue to show that short-term and medium-term local control rates are generally higher than 90% with low toxicity, similar to the previous studies. The main acute toxicity reported in the literature is self-limited nausea and fatigue, followed by radiation dermatitis and enteritis. Reported severe toxicities include nephrotoxicity, duodenal ulcer and skin toxicity, but the overall incidence of all these toxicities is very low (< 5% of patients).

Radical nephrectomy + inferior vena cava thrombectomy is a traditional and effective

treatment for renal cell carcinoma with inferior vena cava tumor thrombus.

The research unit has all the diagnostic and therapeutic conditions involved in the protocol. The level of urology surgery in our hospital is in the lead in China. There are a group of clinical experts specialized in renal cell carcinoma with inferior vena cava tumor thrombus, who can ensure that the enrolled patients receive standard preoperative radiotherapy and surgical treatment.

(II) The purpose of this study is as follows:

To determine the safety of the treatment by the study of preoperative stereotactic radiotherapy combined with surgical treatment of patients with renal cell carcinoma and inferior vena cava tumor thrombus. Main purpose: 1. To identify the acute and late toxicity of radiotherapy. Severe toxicity is defined as grade III-IV toxicity according to Common Terminology Criteria Adverse Events (CTCAE) v4.0. 2.To identify whether the difficulty or risk of surgery is increased after radiotherapy by analyzing perioperative complications, operation time, intraoperative bleeding volume, intraoperative transfusion volume of suspended red blood cells, and postoperative hospital stay. Secondary purpose: Using the follow-up data of the patients to clarify the curative effect of the treatment: 1. For Mayo III-IV classification, it may reduce the difficulty of operation, blood loss, blood transfusion rate and perioperative complications. 2. For Mayo II-IV classification, preoperative radiotherapy + surgery may be better than surgery alone, which prolongs survival and reduces recurrence rate. 3. When the tumor thrombus invades the inferior vena cava wall in a wide range, preoperative radiotherapy can be used to preserve the inferior vena cava vessel wall. The pathological changes of tumors after radiotherapy have been proved to have prognostic significance in other tumors. Tumors such as rectal cancer have clear grading standards, which are divided into 4 grades according to the degree of residual tumor after radiotherapy. This study attempts to initially explore the post-radiotherapy changes of renal tumor thrombus, and judge the prognosis of the tumor according to the different pathological changes.

II. How many people will participate in this research?

Approximately 20 people will participate in this research conducted by our center at Peking University Third Hospital, and approximately 15 people will participate in this research at Peking University Third Hospital.

III. What are the contents of this research?

(I) Study design

This study is a non-randomized controlled study, which is not suitable for blind method. According to the registered clinical trial study "Neo advanced SABR for IVC tumor thrombus in newly diagnosed RCC" retrieved from the clinical trail website, the study sample size was divided into two groups, 15 cases in each group. However, there is only one intervention group in our study. After the intervention, a self-control study will be conducted. The purpose is to focus on the safety and effectiveness of the trial. The sample size is estimated to be 20 cases.

(II) Inclusion and exclusion criteria

Inclusion criteria:

1) Age ≥ 18 years old.

2) Imaging examination of renal cell carcinoma with inferior vena cava tumor thrombus.

3) Inferior vena cava tumor thrombus graded from Mayo II to Mayo IV.

4) Oncologists believe that patients are suitable for preoperative stereotactic ablative body radiotherapy (SABR) to treat inferior vena cava tumor thrombus.

5) Urologists believe that patients are suitable for radical nephrectomy and inferior vena cava thrombectomy to treat renal cancer and inferior vena cava tumor thrombus.

6) ECOG 0-2.

7) Able to complete enhanced CT or enhanced MRI (either one) examination.

8) Able to sign this Informed Consent Form.

Exclusion criteria:

1) Subjects with a history of radiotherapy in the area of renal cell carcinoma or inferior vena cava tumor thrombus.

2) Subjects with a history of preoperative targeted therapy, preoperative chemotherapy, or other related treatments.

3) Subjects with a history of pulmonary embolism.

4) Subjects with severe cardiopulmonary insufficiency, severe arrhythmia, myocardial infarction, angina pectoris, severe coagulation disease, or severe liver disease that cannot tolerate SABR or surgery.

5) Subjects with diseases that severely affect the judgment of patients, such as mental disorders.

(III) Research process

1. Before you are enrolled in the study, the doctor will ask and record your medical history, and perform blood routine test, blood biochemistry test, blood coagulation function test, urine routine test, urinary system enhanced CT, abdominal enhanced MRI, and renal dynamic imaging.

If you are a qualified participant, you can participate in the study voluntarily and sign the informed consent form.

If you are not willing to participate in the study, we will treat you according to your wishes.

2. If you agree to participate in this study and sign the informed consent form, you will accept the examination and process related to the trial according to the protocol to confirm whether you are suitable to participate in this study:

The research content process of this project:

(1) On the 1st day after admission, you will have a pre-radiotherapy location check to complete the pre-radiation preparations;

(2) On the 2-7 days after admission, you will have preoperative radiotherapy;

(3) After 4-6 weeks of rest, on the 1st day of re-admission you will have blood routine test, blood biochemistry test, urine routine test, coagulation function test, enhanced CT of the urinary system, and enhanced MRI of the inferior vena cava;

After the research content of this project, the routine diagnosis and treatment project process:

(4) On the 3rd day of re-admission, complete the pre-operation preparations;
(5) On the 4th day of re-admission, you will receive routine surgical treatment;
(6) On the 1st day after surgery, you will have blood routine, blood biochemistry, urine routine, erythrocyte sedimentation rate, and coagulation function tests to complete the assessment of your recovery after the operation. At the same time, you will receive conventional intravenous medication after surgery.
(7) On the 2nd day after surgery, you will have blood routine, blood biochemistry, urine routine, erythrocyte sedimentation rate, and coagulation function tests to complete the assessment of your recovery after the operation. At the same time, you will receive conventional intravenous medication after surgery.
(8) On the 3rd day after the operation, you will have blood routine, blood biochemistry, urine routine, erythrocyte sedimentation rate, and coagulation function tests to complete the assessment of your recovery after the operation. At the same time, you will receive conventional intravenous medication after surgery.
(9) On the 7th day after surgery, you will have blood routine, blood biochemistry, urine routine, erythrocyte sedimentation rate, and coagulation function tests to complete the assessment of your recovery after the operation.
(10) On the day of discharge after surgery, you will have blood routine, blood biochemistry, urine routine, erythrocyte sedimentation rate, and coagulation function tests to complete the assessment of your recovery after the operation.
(11) Every day after the operation, a urology doctor with a title of deputy chief or above will conduct ward rounds to closely observe your condition. Your postoperative pathology will be evaluated by a professional pathologist;
(12) 3 months, 6 months, 9 months, and 12 months after surgery, please go to the outpatient clinic for follow-up in time, and we will also conduct a telephone follow-up.

3. For the study of discarded tissues after routine clinical surgery / operation: our research materials are from discarded tissues after routine clinical surgery / operation, and the enrollment test will not expand the scope of your surgery / operation, nor will it increase the number of specimens.

4. Drugs or procedures prohibited in the study:
None.

5. What do I need to do to participate in the research?

You must come to the hospital with a copy of the medical record and the medical follow-up form according to the follow-up time agreed by the doctor and yourself (during the follow-up period, the doctor may know your situation by telephone or on-site). Your follow-up is very important because the doctor will judge whether the treatment you received really works and guide you in time.

According to your condition, if you need to take medicines related to renal cancer treatment after surgery, you must follow the instructions of your doctor, and please fill in your medication records in a timely and objective manner. At each follow-up, you must return the unused medicines and their packages, and bring other medicines you are taking, including those that you must continue to take if you have other comorbid diseases.

You cannot use other medicines for kidney cancer during the study period. If you need other treatments, please contact your doctor in advance.

(IV) How long will this research last?

3 months, 6 months, 9 months, and 12 months after surgery, please go to the outpatient clinic for follow-up in time. We will also conduct a 2-year telephone follow-up based on your condition.

You can decide to withdraw from the study at any time without losing any benefits you should have received. However, if you decide to withdraw during the course, taking into account your safety issues, it is possible that a related medical examination will be carried out after withdrawal.

(V) What are the risks of participating in this study?

In addition to the risks in the conventional treatment process (before taking a certain treatment measure, we will explain the risks of the treatment in detail and sign an additional informed consent form with you), participating in this study may have the following risks. At the same time, we have prepared the relevant treatment plan and possible compensation plan:

(1) Radiotherapy injury: the possibility of duodenum, liver, and spinal cord injury.

(2) Radiotherapy toxicity: the possibility of skin toxicity, nausea, loss of appetite, vomiting and diarrhea, weight loss, frequent urination, urgency, pancytopenia, liver failure, and renal failure.

(3) During radiotherapy, the tumor thrombus may become loose, and the proximal end may fall off to the heart, which may cause pulmonary embolism and threaten life, and pulmonary embolectomy may be required.

(4) There may be undiscovered or unpredictable adverse events.

Solution:

(1) If duodenal injury occurs, it may need fasting, rehydration, gastrointestinal decompression, acid suppression, pain relief, parenteral nutrition and other treatment, or even surgery.

(2) If liver damage occurs, hepatoprotective treatment may be required.

(3) If spinal cord injury occurs, it may require diuresis, detumescence, cortisol hormone therapy, and surgery if necessary.

(4) If radiotherapy-related toxicity occurs, we treat it symptomatically.

If you experience any discomfort or new changes in your condition during the study period, or any unexpected situation, regardless of whether it is related to the study, you should notify your doctor in time, and he/she will make judgment and give appropriate medical treatment.

During the study period, you need to go to the hospital on time for follow-up and examinations, which may take up some of your time and may cause trouble or inconvenience to you.

For female subjects:

During the study period, pregnancy brings great risks to unborn children, some of which are unpredictable at present. Therefore, pregnant women will not be recruited as subjects in this study. If you are in childbearing age (including one year after amenorrhea), you will be tested for pregnancy (venous blood should be taken for examination), and the test result must be negative before you can continue to participate in this study. If you have sex, you must agree to take appropriate contraceptive measures during the course of the study and in the following months. If you are pregnant or have unprotected sex during the study, please inform your research doctor immediately.

For male subjects:
Participation in this study may damage your sperm and the children you gave birth to during the study. The damage is currently unpredictable. If you have sex, you must agree to use medically approved contraception during the course of the study and in the following months. Please inform your partner of this risk to the unborn baby. She should understand that if she is pregnant, you need to inform your research doctor immediately, and she should also inform her doctor immediately.

(VI) Drug interactions:
For safety reasons, you must inform the research doctor or nurse of all prescription drugs, traditional Chinese medicine products, over-the-counter drugs, vitamins, natural supplements and other health products you are taking before the start of the study. Be sure to tell your research doctor or nurse before taking these drugs during the study.

IV. What are the benefits of participating in the research?

If you agree to participate in this study, you may have direct medical benefits. For example: 1. Reduce the difficulty of operation, blood loss, blood transfusion rate and perioperative complications; 2. In this study, preoperative stereotactic radiotherapy (SBRT) as an adjuvant surgery may be better than surgery alone, which may prolong the survival time and reduce the recurrence rate; 3. When the tumor thrombus invades the wall of inferior vena cava in a wide range, preoperative radiotherapy can be used to preserve the wall of inferior vena cava.

We hope that the information obtained from your participation in this study will benefit patients with the same condition as yours in the future.

Although there is already evidence that radiotherapy has a satisfactory effect on patients with renal cell carcinoma and tumor thrombus, it can not guarantee that it will be effective for you, and you may not have the above benefits. The preoperative stereotactic radiotherapy (SBRT) is not the only way to treat renal cell carcinoma with venous tumor thrombus. If preoperative stereotactic radiotherapy (SBRT) is not effective for your condition, you can ask your doctor about possible alternative treatment.

V. Alternative medical options?

If you do not participate in this study, you have the following options:

- Surgery alone
- Radiotherapy alone
- Surgery combined with postoperative adjuvant therapy (radiotherapy, chemotherapy, targeted therapy, etc.)
- Palliative treatment

VI. Will my information be kept confidential?

We will keep your research records confidential as required by law. The relevant laws of our country provide guarantees for the security of privacy, data and authorized access. Regarding your research information, we will use a unique number to represent you, and the coded information will be properly stored in Peking University Third Hospital. Your identity will not be disclosed when the research information and data obtained from this study are published in scientific conferences or scientific journals. However, in order to ensure that the study meets the requirements of relevant laws and regulations, your records may be reviewed. The reviewers include the relevant national administrative departments and the Ethics Committee of Peking University Third Hospital. We will make every effort to protect the privacy of your personal medical data within the scope permitted by law.

VII. About research expenses?

The patients are responsible for all the costs of the project. If participation in this study brings potential additional costs to the subjects, the patients will also be responsible for all the costs, and the patients will not be compensated for these costs. The treatment and examination required for comorbidities will not be free.

VIII. What compensation can I get?

You will not be compensated for your participation in this study.

IX. In case of study related injury

Doctors will do their best to prevent and treat the possible injuries caused by this study. If you are injured due to participating in the study, the Department of Urology and Oncology Radiotherapy of Peking University Third Hospital will immediately provide necessary medical care, and bear the cost of treatment and corresponding financial compensation in accordance with related laws and regulations. Please contact director Ma Lulin on 15611908062.

If there are adverse events in clinical trials, the medical expert committee will identify whether they are related to this study. The sponsor will provide the cost of treatment and corresponding financial compensation for the damage related to the trial in accordance with the provisions of China's "drug clinical trial quality management standard".

X. Refusal or withdrawal from the study

Your participation in the trial is voluntary. You can refuse to participate or withdraw from the trial in any way at any stage of the trial without discrimination or retaliation. Your medical treatment and rights will not be affected, but all unused research drugs and devices should be returned. After you quit, we will not collect any new data related to you in the future, and will destroy the research data previously collected and the data withdrawn due to adverse reactions.

If you have serious adverse reactions or your research doctor feels that it is not in your best interest to continue to participate in the study, he will decide to withdraw you from the study. If this happens, we will inform you in time and your research doctor will discuss with you other options you have. If the doctor thinks that the sudden interruption of the trial will affect your health, he may ask you to have a check-up in the hospital before stopping the trial.

XI. Related consultation

If you have any questions related to this study, please contact director Ma Lulin at 15611908062.

If you have any questions related to your own rights and interests, or you want to reflect your dissatisfaction and worries in the process of participating in this study, please contact the Comprehensive Research Ethics Office of Peking University Third Hospital at 010-82265571.

XII. What should I do now?

It's up to you (and your family) to decide whether to participate in the study.

Before you make a decision to participate in the study, please ask your doctor about the relevant questions as many as possible.

Thank you for reading the above materials. If you decide to participate in this study, please tell your doctor and he will arrange all matters related to the study for you. Please keep this information.

XIII. Informing statement

“I have informed the subject of the research background, purpose, procedures, risks and benefits of the clinical study on the safety and effectiveness of neoadjuvant stereotactic radiotherapy combined with surgical treatment for patients with renal cell carcinoma with inferior vena cava tumor thrombus. I have given him / her enough time to read the informed consent, discuss with others, and answer his / her research questions; I have told the subject to contact director Ma Lulin whenever he encounters problems related to the research, and to contact the Comprehensive Research Ethics Office of Peking University Third Hospital whenever he encounters problems related to his own rights / interests, and provide accurate contact information; I have informed the subject that he can

withdraw from the study at any time without any reason; I have informed the subject that he / she will receive a copy of this informed consent form, which contains my signature and his / her signature."

Signature of the researcher who obtained the informed consent_____
Contact telephone number_____
Date_____

XIV. Informed consent statement

"I have been informed of the background, purpose, procedures, risks and benefits of the clinical study on the safety and effectiveness of neoadjuvant stereotactic radiotherapy combined with surgical treatment for patients with renal cell carcinoma with inferior vena cava tumor thrombus. I have enough time and opportunity to ask questions, and I am very satisfied with the answers. I have also been told who I should contact when I have questions, dissatisfaction, concerns or want further information. I have read this informed consent and agree to participate in this study. I promise that the information and test results provided to the researchers are true and valid. I know that I can withdraw from this study at any time without any reason. I have been told that I will be given a copy of this informed consent form, which contains the signatures of me and the researcher."

Signature of the subject_____
Contact telephone number_____
Date_____

When the subject is unable to sign, the following method is allowed:

The relationship between the legal representative and the subject: _____
Signature of the legal representative_____
Contact telephone number_____
Date_____

Press the fingerprint: