Effects of Walking Out From Operating Room on Postoperative Recovery of Patients Undergoing Laparoscopic Total or Partial Nephrectomy.

Study protocol

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After receiving the approval from institutional ethical committees, we will obtain written informed consent from 182 patients undergoing laparoscopic total or partial nephrectomy with American Society of Anesthesiology physical status I and II and aged 18 to 65 years. A sample size of 91 patients in each group was selected by a prior power analysis on the basis of the following assumptions: (1) an absolute reduction in the length of the hospital stay by 1 day, (2) standard deviation 2 days, (3) α=0.05, (4) power 90% and (5) missed follow-up rate 5%

Patients will be excluded if they have severe cardiac diseases (cardiac function grading greater than grade 3/arrhythmia including sick sinus syndrome, atrial fibrillation, atrial flutter, atrioventricular block, frequent ventricular premature, multiple ventricular premature, ventricular premature R on T, ventricular fibrillation and ventricular flutter/acute coronary syndrome), or respiratory failure, or hepatic failure, or renal failure, or diabetics, or body mass index (BMI) $\geqslant$30 kg/m^2 , or patients gastric emptying disorders, or poor blood pressure control (receive regular antihypertensive medical treatment but still have systolic blood pressure > 150 mmHg and/or diastolic blood pressure > 90 mmHg), or have schizophrenia, epilepsy, Parkinson's disease, mental retardation, or hearing impairment, or have thrombosis such as in lower extremity or in vena cava or in renal vein or in other veins, or have neuromuscular disorders affecting lower limb activity, such as myasthenia gravis and cerebral infarction, which cause lower limb muscle weakness, or have contraindications for epidural puncture, or participate in other clinical trials, or refuse to sign informed consent for research.

The randomization will take place before the day of the surgery and the patients will be assigned to either intervention (return to ward by walking) or control group (return to ward by lying on the transporting bed). A stratified randomization with three factors including sex, disease character and age will be performed by statistician to ensure an even spread. The randomization is performed externally using a randomization list prepared by a statistician. This process will be blinded and remote to the investigator. The allocation was communicated by the trial coordinator using

concealed envelopes.

The standardized process of perioperative management are as follow:

1. Preoperatively, all patients do not receive bowel preparation.

2. All patients take oral hydration oral hydration diet 11 hours before entering the operating room and take another oral hydration 2 hours before entering the operating room.

3. Operation bed is warmed by warm blanket before the patient lying down and is kept warm during the operation.

4. An epidural (T9–10) catheter is inserted with a test dose of 1% lidocaine (3ml) . If symptoms of total spinal anesthesia do not appear 5 minutes later, morphine (2mg diluted in 5 ml normal saline) is injected through the epidural catheter .

5. Bispectral Indexes (BIS) is monitored before induction of general anesthesia. General anesthesia is induced by propofol (2-2.5 mg/kg), fentanyl (4μg/kg), and cisatracurium 0.15 mg/kg. The propofol and fentanyl are infused by pump individually. Before the anesthesia induction，dexamethasone （5 mg）is given intravenously to prevent nausea and vomiting after operation, Flurbiprofen Axetil (50mg) is given to decrease postoperative pain and Lansoprazole （30mg） is given to attenuate the gastrointestinal side effects .

6. The ventilation parameters are as follows: fresh gas flow rate 2 L/min, inhaled oxygen concentration 50%, tidal volume 7 ml/kg (ideal body weight) , PEEP 6-8 cmH $_2$O, respiratory frequency 12 times/min(timely adjusted according to the end-expiratory CO2 partial pressure).

7. General anesthesia is maintained by sevoflurane (about 0.8MAC) in combination with remifentanil (0.02-0.08μg/kg/min) and dexmedetomidine (0.2-0.3μg/kg/h) to keep BIS 50±10.

8. Thirty minutes before the end of the operation: (1) 0.2% ropivacaine (7ml) is given through epidural catheter, and then the epidural analgesia pump was connected (formula: 0.2% ropivacaine, background flow 1.5 ml/h, bolus 1.5 ml, lock time 20 minutes); (2) Flurbiprofen Axetil (50mg) is given intravenously;(3) intravenous

palonosetron 0.25 mg to prevent nausea and vomiting;(4) The infusion of dexmedetomidine is stopped;(5) The inhalation of sevoflurane is stopped and the flow of fresh gas is reduced to 0.3-0.5 L/min;(6) The flow of fresh gas is increased to 5 L/min until the skin is sutured in order to speed up the washing of sevoflurane; (7) 0.2% ropivacaine (10ml) is irrigated in the renal fossa prior to surgical closure; (8) After the suture skin is completed, 0.5% ropivacaine (10ml) is used for incision infiltration anesthesia.

9. After surgery, the patient is transferred to post-anesthesia recovery room and evaluated whether fulfilling the criteria for mobilization including stable physiological parameters, clear consciousness, normal level of orientation and muscle strength, and painlessness every ten minutes. If patients fulfill the criteria, they will receive different methods of returning to the ward based on the grouping. In the control group, the patient will return to the ward by lying on the transporting bed. In the intervention group, the patients will be raised to a sitting position for five minutes. If the patients do not complain any discomfort and have stable physiological parameters, they will be encouraged to stand. If standing do not cause any discomfort, they will be encouraged to walk within the range of 5-meter long and 60-centimeter wide. If patients can walk within the range, they will return to the surgical ward by walking. However, if patients in the intervention group cannot sitting, they will return to the surgical ward by lying on the transporting bed. If patients can sit but cannot stand or walk, they will return to the surgical ward by sitting in the wheel chair.

Then, all study patients will be subject to the same management such as the guidance of drink and diet recovery, the guidance of mobilization in the ward (the duration and distance of walking in the ward will be recorded every day), nutrition supplement after surgery, and the criteria of drainage removal and hospital discharge. The outcomes such as the length of hospital stay after surgery will be recorded and analyzed to evaluate the effects of walking out from the operating room.

Recovery time, which is considered an ideal time point for discharge. The criteria for measuring recovery time included: 1) tolerance of diet and not necessary for

intravenous nutrition; 2) analgesic-free, which is defined as visual analogue scale $\leqslant 3$ without intravenous analgesic drugs, 3) adequate mobility; 4) afebrile status without major infectious complications (fever is defined as body temperature greater than 37.2°C at axilla). Patients is discharged when they consider themselves sufficiently recovered after the recovery time.

Statistical analysis Mean (SD) for normally distributed data or median (Q1, Q3) for skewed data will be calculated for continuous variables, and frequency (percentage) will be generated for nominal or ordinal variables. As to inferential analysis, continuous variables will be analyzed with Student's t test or Mann-Whitney U test or Analysis of Variance for Repeated Measures. Mann-Whitney U test will also be used to the ordinal variables. Categorical outcomes will be analyzed with χ^2 test or Fisher's exact test. The analysis of Intention-to-treat and Per-protocol sets will be both performed by statisticians.