Trials

STUDY PROTOCOL

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Open-label randomised clinical trial investigating whether robot-assisted kidney transplantation can reduce surgical complications compared to open kidney transplantation (ORAKTx): study protocol for a randomised clinical trial

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Abstract

Background Kidney transplantation is the ultimate treatment for end-stage kidney disease. Function of the kidney graft is not only dependent on medical factors but also on a complication-free surgical procedure. In the event of major surgical complications, the kidney graft is potentially lost and the patient will return to the waiting list which may be long. To optimise peri-operative care and reduce complications, robot-assisted kidney transplantation (RAKT) has been introduced as an alternative to open kidney transplantation (OKT), but to our knowledge, no randomised clinical trials (RCT) have compared RAKT to OKT. In this study, we will explore whether robot-assisted surgery can reduce 30-day surgical complications compared to open surgery in kidney transplantation.

Methods This is a single-site, open-label, randomised clinical trial comparing RAKT to OKT. Participants are adult recipients of kidney transplantation recruited from Copenhagen University Hospital – Rigshospitalet, Denmark. The study plans to include 106 participants who will be randomised in a 1:1 manner between OKT and RAKT. Primary outcomes are vascular- and major surgical complications at 30 days post-operatively. Participants will be followed for 2 years to evaluate secondary outcomes including recovery, late complications and kidney graft function. This is designed as a superiority trial and planned analyses will follow intention-to-treat principles.

Discussion Studies indicate RAKT can reduce several surgical complications, but the lack of RCTs limits the extrapolation of these results to justify replacing an open approach with a robot-assisted one. Ultimately, the introduction of new surgical techniques should be as vigorously tested as any other new treatments. However, reducing surgical complications that compromise graft viability could lead to improved patient care and survival.

Trial registration The trial was prospectively registered with *ClinicalTrials.gov* on February 15th, 2023, with the identifier NCT05730257.

Keywords Kidney transplantation, Robotic surgery, Urology, Randomised controlled trial, End-stage renal disease

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Administrative information

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Role of sponsor {5c}	AR serves as sponsor-investigator.

Introduction

Background and rationale {6a}

Kidney transplantation is the best treatment for suitable patients with end-stage kidney disease both in terms of survival and quality of life (QOL) [1]. It is also a high-risk procedure demanding expert medical knowledge and excellent surgical skills while operating on a comorbid patient group prone to complications during any surgical procedure [2–4]. Surgical complications negatively affect patient recovery, compromise graft survival and feel particularly catastrophic in the setting of live-donor transplantation [5]. Urological complications are among some of the most frequent surgical complications following kidney transplantation, with reported incidences ranging from 6.5% to as high as 20.8% [6, 7]. While these complications rarely affect graft survival, they often require intervention such as reoperation or permanent ureteral stenting. Conversely, vascular complications such as renal artery and vein thromboses are relatively rare with reported rates from 1.5 to 4.8%, but directly and dramatically reduce graft survival [8–10]. Other significant vascular complications include renal artery stenosis, bleeding and haematomas around the graft, but with definitions varying across studies, reported rates likewise range from anywhere as high as 19.7% to as low as 4.0% [9–11]. Many of these vascular complications can be attributed to the technical aspects of the vascular anastomoses.

In contrast to immunosuppressive therapy and the field of surgery in general, the surgical technique in kidney transplantation has not developed significantly during the past 50 years and the standard of care remains open kidney transplantation (OKT) [12–14]. The introduction of robot-assisted surgery in other selected procedures

has led to reduced complications, enhanced recovery and an expanded pool of surgical candidates including those with severe obesity [15, 16]. To obtain the benefits of minimally invasive surgery in the transplant setting, robot-assisted kidney transplantation (RAKT) has been implemented in several European centres [17, 18]. Studies show that RAKT has a very low rate of lymphoceles and surgical site infections, while kidney function outcomes seem non-inferior to OKT [17]. This has led to speculation that RAKT holds the potential to further reduce complications compared to OKT [19]. However, this needs to be explored in an RCT, and currently, there is no such trial published.

Objectives {7}

The trial aims to investigate whether robot-assisted surgery can reduce early surgical complications following kidney transplantation compared to open surgery. We hypothesise that RAKT can reduce vascular- and major surgical complications within 30 days of surgery compared to OKT. Additionally, we will explore the patient trajectory following the two procedures in terms of recovery, late complications and graft function.

Trial design {8}

The study design is a superiority, open-label randomised clinical trial comparing RAKT to OKT. The study will randomise 106 participants between the two procedures in a 1:1 allocation ratio.

Methods: Participants, interventions and outcomes

Study setting {9}

Participants are recruited from the Department of Nephrology and Department of Urology at Copenhagen University Hospital – Rigshospitalet. The combined departments are responsible for the living- and deceased donor kidney transplantation programme in Eastern Denmark. Approximately 100 kidney transplantations are performed every year, of which 30% are living donors. The Department of Urology is a centre of excellence in robotic surgery, performing advanced abdominal surgery with DaVinci X ® and HUGO RAS ® surgical systems and it is the only centre in Denmark that performs robot-assisted kidney transplantation.

Eligibility criteria {10}

Study participants

All kidney recipients undergo standard work-up prior to transplantation according to the KDIGO guidelines [20]. Study eligibility is assessed at the pre-transplant urological evaluation. In addition to standard work-up, trial participation can in some instances require a non-contrast CT of the abdomen to exclude severe calcification of the iliac vessels at physician discretion (see exclusion criteria below).

Inclusion criteria

- Adult recipients for renal transplantation
- Both patients in dialysis as well as pre-emptive

Exclusion criteria

- High degree of calcification of the iliac vessels on the level of the external iliac artery defined as the occurrence of longitudinal plaques on non-contrast CT scan or other relevant radiological imaging in the recipient prior to transplantation
- Highly complex vascular anatomy in the donor kidney requiring multiple anastomoses as evaluated by the surgeon
- Previous kidney transplantation with later allograft nephrectomy as evaluated by the surgeon preoperatively
- Patients whose abdominal anatomy may prohibit access to and placement of the graft in the iliac fossa as evaluated by the surgeon preoperatively (i.e. previous laparotomy, rectal surgery, herniotomy, current multiple kidney cysts).
- Simultaneous multiple organ transplant
- Severe comorbidities contraindicating robot-assisted surgery
- Patients who are unable to understand relevant medical information and the implications of treatment alternatives and to make an independent, voluntary decision

For recipients of kidneys from deceased donors, additional exclusion criteria must be evaluated at index hospitalisation. This includes vascular graft anatomy as described above and the availability of 1) the robotic operating room and 2) the dedicated surgical team.

Participating surgeons

OKT: Surgeons at Rigshospitalet who perform kidney transplantation independently are eligible to participate in the study. They are all senior consultants experienced in the procedure.

RAKT: Surgeons at Rigshospitalet who perform RAKT independently are eligible to participate in the study as surgeons of both interventions. They are highly experienced in both open- and robot-assisted surgery, as well as kidney transplantation.

Who will take informed consent? {26a}

The treatment-responsible urologist assesses if the patient is eligible for study participation based on the inclusion/exclusion criteria. If the patient is eligible, they are informed of the possibility of being included in the study and relevant written study material is made available. If the patient gives oral consent, the personal information is passed on to the study team and the patient is invited for a meeting. The patient is informed about the right to have a family member or an acquaintance present at the meeting, during which the trial's advantages, disadvantages and side effects are discussed in detail. The patient is offered a minimum of 24 h of decision time, assuming the transplantation process allows it. If the patient wishes a prolonged decision period, a new appointment is arranged. If oral consent is given, a study representative trained in the process obtains written consent for patient participation.

Additional consent provisions for collection and use of participant data and biological specimens {26b}

N/A, no additional consent is necessary.

Interventions

Explanation for the choice of comparators {6b}

According to the European Association of Urology (EAU), the standard surgical approach to kidney transplantation remains open surgery [14]. Aside from the possible benefits of minimally invasive surgery, RAKT also offers a magnified image and added degrees of freedom of the surgical instruments during vascular suturing, both of which may improve the quality of the vascular anastomoses.

Intervention description {11a}

Both procedures take place after the preparation of the graft on the organ back table and with the patient under general anaesthesia administered intravenously. Peri-operative medications include mannitol 150 mg/ml (300 ml), furosemide (120 mg) and piperacillin/tazobactam (4 g/0.5 g). A baseline biopsy of the graft is performed at the back table for comparison in case of later graft failure. At the end of surgery, intravenous oxycodone is administered and a local anaesthetic in the incisions is administered by the surgeon. An indwelling bladder catheter is placed and removed after 5 days.

ARM 1 (control group): open kidney transplantation

A Gibson incision is performed in the right or left iliac fossa and the peritoneum is displaced. With the kidney under hypothermia, the iliac vascular bed is prepared, the vessel lumens flushed with heparin and a vascular clamp instrument is used to block the vessels during suturing. The kidney graft vessels are anastomosed end-to-side to the external iliac vessels using a monofilament synthetic non-absorbable suture 6–0. The ureterovesical anastomosis is performed ad modem Woodruff with a 4–0 synthetic monofilament suture with delayed absorption and a ureteric JJ stent in the ureter. The graft is placed in the cavity, the fascia is closed in layers using a 2–0 synthetic absorbable polyglactin suture and the skin is closed using a monofilament, synthetic resorbable suture intracutaneously. The JJ stent is removed after 2 weeks.

Arm 2 (intervention group): robot-assisted kidney transplantation

A small Pfannenstiel incision is performed through which a hand-port is placed and pneumoperitoneum is obtained. Ports are placed under visual guidance according to a pre-specified scheme. The patient is placed in 20-degree Trendelenburg, the DaVinci® robot is placed between the patient's legs and docked to the ports. The iliac vascular bed is prepared and a peritoneal cavity is created laterally. The kidney is introduced through the hand port under regional hypothermia obtained via ice slush in the cavity. The vessel lumens are flushed with heparin and vascular clamps are used to block the vessels during vascular suturing. The vascular anastomoses are performed end-to-side to the external iliac vessels using a Gore-Tex® non-absorbable suture 6–0. The kidney is placed in the retroperitoneal cavity, the ureter is placed extra-peritoneally and the ureterovesical anastomosis is performed ad modem Woodruff, with a 4–0 or 5–0 synthetic monofilament suture with delayed absorption and a JJ stent in the ureter. The fascia in the Pfannenstiel is closed in layers using a 2–0 synthetic absorbable polyglactin suture and the skin is closed using a monofilament, synthetic resorbable suture intracutaneously. The JJ stent is removed after 2 weeks.

Criteria for discontinuing or modifying allocated interventions {11b}

The discontinuation of allocated treatment is not expected as this is a one-time surgical intervention. Participants can withdraw consent at any point in time. If withdrawal occurs prior to surgery, patients receive the standard of care (OKT) outside of study participation. A surgeon performing RAKT may be forced to convert to open surgery if complications arise peri-operatively, as is always the case with laparoscopic surgery. In such cases, the participant remains in the allocated arm for analyses.

Strategies to improve adherence to interventions {11c}

N/A: the intervention is surgical.

Relevant concomitant care permitted or prohibited during the trial {11d}

There are no restrictions regarding concomitant care. All participants will be managed according to the standard protocols for anaesthesia and renal transplantation at Rigshospitalet. This includes an individually tailored immunosuppressive regimen determined by a nephrologist according to local guidelines. Recipients of RAKT have their anaesthetic protocol tailored to suit robot-assisted surgery per local guidelines.

Provisions for post-trial care {30}

Patients will not receive compensation, monetary or otherwise, for their participation in the trial.

Study participants are followed lifelong in a nephrological department like all other kidney recipients. All Danish citizens have equal access to the healthcare system through a publicly funded compensation scheme. In case of harm suffered due to participation, The Danish Patient Compensation Law applies (Patienterstatningsloven).

Outcomes {12}

The trial measures two primary outcomes which are both assessed through an in-depth review of the patient's electronic health record (EHR):

1. Vascular complications < 30 days of surgery. This is a composite outcome related to the graft vessels consisting of: vascular thrombosis, arterial stenosis, symptomatic haematomas and bleeding requiring re-operation.
2. Major surgical complications < 30 days of surgery. A surgical complication is defined as'any deviation from the normal post-operative course' that is not a failure to cure or sequelae inherent to the procedure (per Clavien-Dindo). Major is defined as *higher than* grade two [21].

Both these measures constitute patient-related major clinical events that can impact short-term graft survival and will greatly benefit recipients of kidney transplantation if reduced.

Secondary outcomes measure three overall topics: recovery, graft function and late complications. All except QOL, are assessed through an in-depth review of the patient's EHR. The timepoint of assessments (from the date of surgery) is addressed at the end of each outcome.

Recovery

- Length of stay (LOS) in days, index hospitalisation
- Use of opioids post-operatively (in morphine milligramme equivalents per day), index hospitalisation
- Transfusion rate with red blood cells (units), 30 days
- Days alive and out of hospital (DAOH), 30 and 90 days
- Time to return to work (weeks), 90 days
- Patient-reported health-related QOL using the 36-item short-form survey (SF-36), 30 and 90 days
- All-cause mortality rate and cause of death, 30 days

Graft function

- Delayed graft function
- Kidney function (estimated glomerular filtration rate and serum creatinine), 30 and 90 days, 1 and 2 years
- Occurrence of rejection and Banff classification when appropriate, 1 year
- Occurrence of graft loss: 30 and 90 days, 2 years

Late complications

- Recurrent urinary tract infections, 90 days, 2 years
- Urological complications 30 and 90 days, 2 years
- Mortality rate and cause of death, 90 days, 1 and 2 years

Table 1 summarises all outcomes including definitions and units.

Recovery

LOS is commonly used as an objective but surrogate measure of patient recovery after a surgical procedure but does not cover readmissions, which is accounted for in DAOH [24]. The use of opioids post-operatively is directly related to post-operative pain and can be used as a surrogate marker for recovery. Transfusion with red blood cells is a common complication following kidney transplantation and can, to a certain extent, reflect non-significant bleeding as well as worsening of pre-operative anaemia due to fluid resuscitation. Time to return to work and QOL directly reflect the patient experience and the SF-36 is both validated and commonly used in the kidney transplant population [1, 25].

Graft function

Function of the kidney is the ultimate goal in kidney transplantation. Delayed Graft Function (DGF) can be measured within a week of transplantation and is to some degree indicative of long-term function [26]. Rejection and graft loss represent long-term markers of kidney function (or lack thereof).

Late complications

Urological complications defined as lymphoceles, extravasation of urine, ureteric strictures and hydronephrosis are

Table 1 Summary and definitions of primary and secondary outcomes

Post-operative outcome assessments	
Outcome	**Definition**
Primary	**< 30 days**
Vascular complications	A graft-related composite outcome of renal vascular thrombosis, renal artery stenosis, symptomatic haematomas and bleeding requiring reoperation[d]
Major surgical complications	Any deviation from the normal post-operative course that is not a failure to cure or sequelae inherent to the procedure and major is defined as *higher than* grade two according to Clavien-Dindo
Secondary	**Recovery**
Length of stay (LOS)	Date of surgery until day of discharge to own home, including transfers to other departments (days)
Days alive and out of hospital	30 – (LOS + length of readmission[a] + days dead before post-operative day 30[b])
DAOH [22]	90 – (LOS + length of readmission[a] + days dead before post-operative day 90[b])
Use of analgesics (MME/day)	Average administered daily dose of any opioid agent in morphine milligramme equivalents (MME) post-surgery, during in-hospital stay (LOS)
Transfusion rate	Total amount of red blood cells administered (units)
Time to return to work	Time in weeks from operation until any degree of work is resumed. Includes full-time students
Quality of life (SF-36)	Patient-reported health-related quality of life using the 36-item short-form health survey
	Late complications
Recurrent urinary tract infections (UTI)	Culture-confirmed recurrent UTI as defined by EAU guidelines[c]
Urological complications	Ureteral strictures, hydronephrosis, symptomatic lymphocele, extravasation of urine; including, when needed, designated intervention (bladder catheter, JJ stent, nephrostomy, drain, surgery)[d]
Mortality	Mortality rate and cause of death
	Graft function
Delayed graft function	Need for dialysis in the first post-operative week beyond day 0, due to lack of increase in kidney function and where the cause is not urological/surgical complications or hyperkalaemia alone
Kidney function	Plasma creatinine and estimated glomerular filtration rate (eGFR). Creatinine: µmol/L. The eGFR is calculated according to the CKD-EPI equation
Rejection	Occurrence of graft rejection and diagnostic category according to Banff Classification of Renal Allograft Pathology if appropriate [23]
Graft loss	Occurrence of graft loss defined as start of permanent dialysis and/or allograft nephrectomy

[a] Length of readmission calculated from the date of readmission until the date of discharge. Patients readmitted and discharged on the same date are recorded as having length of readmission 1 day

[b] Days dead before post-operative day 30 or 90 calculated as the date of post-operative day 30 or 90 minus the date of death

[c] EAU Guidelines define recurrent UTI as a frequency of at least three UTIs in 1 year or two in the last 6 months

[d] Please refer to Additional file 1 for definitions of each complication

some of the most frequent surgical complications in kidney transplantation [6, 27]. They rarely affect graft survival but often require intervention, which is of great cost to both patients and the healthcare system. Recurrent urinary tract infections are a frequent, long-term complication of kidney transplantation [28]. Short- and long-term mortality rates are essential to monitor in any interventional trial.

Participant timeline {13}

During the pre-transplant urological evaluation, the inclusion/exclusion criteria are assessed to determine whether the patient is eligible to be included in the study. Information on the patient demographics and medical/surgical history relevant to the procedure is registered in the EHR. For recipients of kidneys from deceased donors, the inclusion/exclusion criteria are evaluated by the treatment-responsible urologist at the time of admission for transplantation.

Participants are randomised once informed consent is obtained and time of surgery is known. Intra-operative data and graft data are registered in the EHR at the time of surgery. Table 2 demonstrates the recipient, donor, graft and intra-operative variables collected.

The normal post-operative course for kidney transplant recipients is transferred to the Department of Nephrology after a short-term stay in the post-operative care unit. This includes regular ultrasound to assess graft function and urology consults as needed. Discharge typically occurs after 1 to 3 weeks with a median LOS of 11 days. After discharge, recipients attend outpatient visits at the Department of Nephrology twice a week in the first post-operative month. Hereafter, recipients are followed according to an individual evaluation based on their health status. All recipients are seen at least once every year until death. Study participants will follow the same regimen. In

Table 2 Intra-operative, recipient, donor, and graft variables

Recipient
Age
Sex
Body mass index
Charlson Comorbidity Index (adjusted for chronic kidney disease) [29]
Baseline renal disease
Previous dialysis and type
Immunosuppressive regimen
Previous abdominal surgery
Social status
Employment status
ABO compatibility
Donor[a]
Age
Sex
American Society of Anaesthesiologists physical status I–V (living donors)
Donor type (living/deceased)
Graft[a]
Results of crossmatch analyses
Kidney side
Graft anatomy
Ischaemia times
Use of perfusion machine
Baseline biopsy results
Intra-operative data
Total operative time (from first incision to closure)
Total fluid resuscitation
Total blood loss
Major adverse events (bleeding > 1L, organ perforation, loss of graft, death of patient)
Conversion to open surgery
Surgeon (anonymised)
Recipient haemodynamics
Suture used for anastomoses (type and size)

[a] If available: The Department of Urology Rigshospitalet is part of the ScandiaTransplant kidney Exchange Program and therefore receives kidneys from other countries. Information on donors from kidneys harvested abroad is not always available

addition, they will electronically receive questionnaires regarding QOL at approximately 30- and 90-days post-operatively. Follow-up for study purposes will cease after 2 years.

All assessments and variables, except QOL, are obtained through an in-depth review of the EHR which contains both in-hospital and out-patient data. Figure 1 schematically demonstrates the participant timeline.

Sample size {14}

To estimate the number of participants needed to detect the two primary outcomes a power calculation was performed using the statistical analyses program R version 4.2.1 (R Development Core Team, Vienna, Austria) running on RStudio version 2022.07.01 (© 2009–2022 by RStudio, Inc). The calculation yielded a sample size of 106 participants with an anticipated drop-out of 10% ($n = 96$).

1. The current rate of vascular complications for OKT is 17.3% [30]. With a power set at 80% and a significance level set at 5%, we hypothesise that RAKT will lead to an absolute reduction in vascular complications of 15% within 30 days of transplantation compared to OKT.
2. The current rate of major surgical complications (Clavien-Dindo grade > 2) is 22.8% [30]. With a power set at 80% and a significance level set at 5%, we hypothesise that RAKT will lead to an absolute reduction in Clavien-Dindo > 2 of 20% within 30 days after transplantation compared to OKT.

Based on having two primary outcomes, we did not adjust our significance level for sample size calculations as they were deemed of equal importance to determine the risk and benefit of both procedures. As such, the number of the sample size is defined by having the power to prove the significance of the primary outcome requiring the largest number of included patients. The anticipated reduction in vascular complications required the largest sample size with 48 participants in each arm (to a total of 96, with an added 10% drop-out = 106). The anticipated reduction in major surgical complications required 34 participants in each arm (to a total of 68, with an added 10% drop-out = 75).

The anticipated drop-out rate of 10% was chosen to account for any participants where outcome data will not be available while ensuring adequate power is maintained. At Rigshospitalet transplantation is performed in patients from the Faroe Islands and Greenland, which do not allow access to the EHR. While the majority of these patients are not expected to travel home before the 30-day primary outcomes, it may affect the long-term outcomes as the date of return is not predetermined and depends on the post-operative course. Drop-outs, in this sense, refer to these participants who live in the Faroe Islands or Greenland as well as those who withdraw both consent and data or move away from Denmark.

Recruitment {15}

All recipients undergo urological evaluation prior to kidney transplantation. The criteria for study eligibility are broad and representative of the general kidney recipient population. Physicians involved in transplantation at the Department of Urology regularly receive instructions

Timeframe	Pre-operative		Peri-operative	Post-operative				
Enrolment & assesments	**Pre-transplant urological evaluation**	**Index hospitalisation**	**POD 0**	**POD 0 - discharge**	**POD 30**	**POD 90**	**1 year**	**2 years**
Enrolment								
Eligibility screen	x——	x						
Informed consent	x——	x						
Medical & surgical history, demographics of recipient & donor	x	x						
Allocation		x——	x					
Non-contrast CT	x——	x——	x					
Final exclusion criteria evaluated for recipients of kidneys from deceased donors (graft anatomy & availabilty of robotic operating room & dedicated surgical team)		x	x					
Intervention (OKT or RAKT)			x					
Intra-operative data			x					
Graft data		x——	x					
Adverse events			x	x	x			
Primary outcomes								
Vascular complications					x			
Major surgical complications					x			
Secondary outcomes								
Recovery								
Transfusion of red blood cells					x			
Use of opioids				x				
Length of stay				x				
Days alive and out of hospital					x	x		
Time to return to work						x		
Quality of life (SF-36)					x	x		
Late complications								
Recurrent UTI						x		x
Urological Complications					x	x		x
Mortality rate & cause of death					x	x	x	x
Graft Function								
eGFR & serum creatinine					x	x	x	x
Graft loss					x	x		x
Rejection & Banff Classification						x	x	
Delayed graft function				x				

CT: computed tomography, eGFR: estimated glomerular filtration rate, KTx: kidney transplantation, MME: morphine milligram equivalents, OKT: open kidney translantation, POD: Post-operative day, RAKT: robot-assisted kidney transplantation, UTI: urinary tract infection

Fig. 1 Participant timeline

about the ongoing study. Likewise, both physicians and staff at the Department of Nephrology were trained prior to the study commencing. The enrolment period is expected to be 2.5 years and inclusion in the study will cease after 106 participants have undergone operation.

Assignment of interventions: allocation

Sequence generation {16a}

Randomisation is performed using the randomisation module in the Research Electronic Data Capture software (REDCap). Prior to trial initiation, a collaborator with no clinical involvement has generated a sequence of random numbers using R version 4.2.1. The sequence uses differing block sizes unknown to other study members. The sequence was uploaded to REDCap prior to trial initiation and can neither be viewed, nor changed. No form of stratification is used.

Concealment mechanism {16b}

As described above investigators were not involved in the generation of the allocation sequence which was

uploaded to REDCap prior to trial initiation and can neither be viewed, accessed, nor changed through REDCap by those enrolling. Investigators are not aware of the location of the sequence, but the collaborator who generated the sequence will provide it upon study conclusion.

Implementation {16c}

Participants will be randomised with a 1:1 allocation ratio, and pre-surgery drop-outs will be replaced by the same randomisation number to ensure equal distribution. Pre-surgery drop-outs refer to patients who are randomised but do not undergo any surgery. The investigators perform the randomisation once informed consent is obtained, radiological evaluation of vascular calcification is available and the time of surgery is known.

Assignment of interventions: blinding

Who will be blinded {17a}

This is an open-label trial; the allocated treatment will be known to study personnel, patients and outcome assessors.

Procedure for unblinding if needed {17b}

N/A: This is an open-label trial; both study personnel, patients and outcome assessors will be aware of the allocated treatment.

Data collection and management

Plans for assessment and collection of outcomes {18a}

All outcomes and variables are collected via the EHR by the trial physician. The EHR contains both in-hospital and outpatient information as well as all peri-operative data. Complications that arise during out-patient follow-up will be included if they are judged to be related to surgery by the assessor but death within 30 days of surgery is always considered a grade 5 surgical complication per the Clavien-Dindo taxonomy. Any cases of doubt are first discussed with a co-author (JD) who is experienced in assessing surgical complications following OKT and subsequently the PI. The trial physician will train potential subsequent assessors.

QOL surveys are distributed electronically via REDCap to a protected personal email where Danish citizens receive all official mail. They are likewise returned electronically to REDCap via a confidential personal survey link.

Plans to promote participant retention and complete follow-up {18b}

We expect participant retention to be high because the study does not require extra visits. All hospitals in the capital and neighbouring region of Denmark use the same EHR system and potential loss to follow-up will only include participants who move outside of these regions during the study period.

Data management {19}

All data are collected in standardised electronic case report forms in a REDCap database specifically developed for the trial. Access to the database requires twofold password identification and assignment by the investigators. Quality of data is ensured using the built-in features of REDCap including validation of the entered unit/measurement; range checks for values and dates; missing data warnings and branching logic. The calendar function allows for the follow-up of individual participants at the planned timepoints of assessment.

Confidentiality {27}

Personal data are stored electronically in accordance with the Danish Data Protection Regulation (Databeskyttelseforordningen), the Danish Data Protection Act (Databeskyttelseloven) and the Danish Health Law (Sundhedsloven). Data are also available to third parties for control purposes (external monitoring, quality control, etc.) in accordance with Danish law. Data can be extracted from REDCap without personal identifiers and will be stored in a pseudo-anonymised form on a secured logged drive at a server at Rigshospitalet.

Plans for collection, laboratory evaluation and storage of biological specimens for genetic or molecular analysis in this trial/future use {33}

N/A: no biological material will be collected and/or stored for the purpose of the study.

Statistical methods

Statistical methods for primary and secondary outcomes {20a}

The planned analyses will follow intention-to-treat, meaning all participants who are randomised and undergo surgery will be analysed according to the allocated treatment group—regardless of which intervention they receive and whether or not the transplantation is successful. This also includes any robotic cases that may be converted to the open approach.

Given the unique situation of transplantation where the intervention involves both surgery and the allocation of an organ through an official waiting list, pre-surgery drop-outs (patients who are randomised but do not undergo any surgery), are not included in the intention-to-treat analysis. This decision was made because these patients will by definition never experience any of the primary outcomes (post-operative complications). Furthermore, it would not reflect future clinical practice because

an organ can only be allocated once, and patients who are not transplanted do not receive either intervention. These cases are interpreted as premature randomisation, as described by Fergusson D. et al. regarding post-randomisation exclusion and can reasonably be left out of the intention-to-treat analysis without biasing results [31].

This will expectedly come to a very small number as living donor transplant recipients are extremely well vetted before surgery is planned and deceased donor transplant recipients are naturally randomised in extreme proximity to surgery. Any such cases will be presented in the consort flow chart for transparency.

The primary outcomes are expected to be evaluated as the proportion of patients with complications compared between the two groups using the exact binomial test. A level of 5% is considered statistically significant.

Secondary outcomes will be presented descriptively and analysed according to the data type using either Student's *t* test or the exact binominal test. Multiple testing will be accounted for as per the Benjamini-Hochberg (false discovery rate) procedure. Statistical analyses will be undertaken using R version 4.3.1 or later if available. In case of deviations from the statistical analysis plan, the information on ClinicalTrials.gov will be updated.

Interim analyses {21b}

An interim analysis on primary outcomes will be performed when 50% of participants are enrolled. This is to ensure participants do not suffer unnecessary harm due to trial participation and to evaluate if the study hypothesis has been confirmed earlier than the power calculation indicated, rendering further trial conduct unnecessary. In case of the rate of complications in the control group being significantly lower than anticipated in the power calculation, a new power calculation will be undertaken to indicate if the sample size needs to be re-evaluated. The PI determines if the trial needs to be terminated earlier than planned or otherwise altered.

Methods for additional analyses (e.g. subgroup analyses) {20b}

Subgroup analyses for exploratory purposes will be performed according to 1) AB0-compatibility (compatible vs. incompatible) and 2) donor type (living vs. deceased).

The analyses are expected to be in the form of adjustments in a logistic regression model, including testing for interaction assumptions.

Methods in analysis to handle protocol non-adherence and any statistical methods to handle missing data {20c}

Protocol non-adherence is expected to be insignificant as this is a one-time surgical intervention. Likewise, missing data is expected to be low as explained in item 18b and analyses are expected to be performed on complete cases. Any cases of conversion from robotic to open surgery, loss to follow-up or non-adherence will be presented descriptively.

Plans to give access to the full protocol, participant-level data and statistical code {31c}

The full protocol, data collection instruments, participant-level data and the statistical code are not made publicly available. They can be delivered upon reasonable request by contacting the PI or the corresponding author, but access to participant-level data (in a de-identified form) requires approval from the Danish Data Protection Agency.

Oversight and monitoring

Composition of the coordinating centre and trial steering committee {5d}

As this is a single-site study, the trial investigators are handling all aspects of trial management from monitoring enrolment and training of study staff to checking data quality. The PI, Coordinating Investigator and Head of Department of Urology are in continuous contact and collectively manage the day-to-day aspects of the trial. Departments of Nephrology and Urology have weekly meetings where any issues related to the transplantation process can be discussed. The complete investigator group attends regular meetings to discuss trial progress and challenges.

Composition of the data monitoring committee, its role and reporting structure {21a}

A data monitoring committee was deemed unnecessary as this is a single-site study and data entry is performed by the trial investigators. Based on the available literature on both procedures prior to trial initiation, an external safety assessment was likewise deemed unnecessary.

Adverse event reporting and harms {22}

Assessment of severe adverse events (SAEs) occurring from surgery until follow-up at 30 days is evaluated through a review of the EHR by the trial physician. All SAEs are reported within 7 days to the PI who reviews the received reports. In case of unexpected serious adverse events, the ethics committee is notified immediately upon awareness and no longer than 7 days later. In addition, the ethics committee will receive safety reports annually and within 90 days of study termination or completion.

Frequency and plans for auditing trial conduct {23}

The ethical committee responsible for approval can spontaneously audit trial conduct, independently of investigators and the sponsor.

Plans for communicating important protocol amendments to relevant parties (e.g. trial participants, ethical committees) {25}

In case of substantial protocol modifications, these will be reported immediately to the ethics committee which will review and approve the changes. All potential modifications will be tracked and dated.

Dissemination plans {31a}

All results regardless of outcome will be made available by publication in peer-reviewed international journals, presentation at conferences or other public access. The trial is registered at www.ClinicalTrials.gov. No information exposing participant identity will be publicised.

A layperson summary of results will be sent electronically to participants upon trial termination, if requested in their consent form.

Discussion

Patients on the waiting list for kidney transplantation often have severe systemic disease and the medical history can entail years of treatment for complications due to lack of kidney function and dialysis. At baseline, these patients have a high risk of complications to any surgery which pinpoints how vulnerable their situation is prior to a life-changing transplantation [2, 4]. Successful kidney transplantation is not only mediated through optimal medical care but also through minimising surgical complications where the technical aspects of performing the vascular anastomoses are a key factor.

Despite variations in the reporting of surgical complications following kidney transplantation, there is still a high incidence of complications that can affect graft survival, demonstrating the continuous unmet need to improve surgical outcomes in this setting. Particularly vascular complications play a major and immediate role in graft function, length of stay and other patient-related factors such as post-operative pain or infection from a large haematoma surrounding the graft [10]. Additionally, late urological complications such as ureteral strictures may develop and affect late graft function. More importantly, these are problematic for the individual patient with a need for permanent nephrostomy or JJ stent [6].

Minimally invasive surgery is known to have lower rates of bleeding in standard patients and surgery on the ureter, e.g. neo-implantation or pyeloplasty, is rarely performed with open surgery today [16, 32]. Robot-assisted surgery could offer advantages in kidney transplantation and reduce complication rates through the minimally invasive nature of the procedure as well as the technical advantages of performing both anastomoses. However, although deemed safe in several surgical cas series, this dogma must be tested in a randomised clinical trial [19].

The intent of the study is to perform a pragmatic RCT, reflective of the real-life clinical world in our transplantation unit. We include a broad cohort of participants representative of the kidney transplantation community including recipients with a history of abdominal surgery, previous transplantation and recipients of both living- and deceased-donor kidneys [27]. Our primary outcomes are patient-related, major clinical events that greatly affect patient recovery and/or graft survival. Further strengths lie in our predefined procedure-specific complications, use of a standardised severity grade and assessment of primary outcomes through chart review, instead of relying on diagnostic codes notorious for underreporting complications [33].

One of the many challenges surgical RCTs face is the influence of surgeon performance on outcomes [34, 35]. We have sought to limit the potential implications of differences in surgical skills by restricting participating surgeons to senior consultants with extensive surgical experience who already perform kidney transplantation independently, keeping in mind volume and experience are determining factors for surgical outcomes [16, 36]. Our RAKT surgeons are experienced in kidney transplantation, open surgery and robotic surgery. While their experience with RAKT was limited at trial initiation, studies indicate that previous experience with both kidney transplantation and robotic surgery is determining in reaching attenuation of the learning curve which may even be rendered non-significant [37, 38]. Furthermore, including recipients of kidneys from deceased donors in the study poses a logistical challenge due to the limited capacity of the robotic operating room and staff. However, we have already included several recipients of deceased-donor kidneys demonstrating feasibility.

There are several limitations to this RCT which must be addressed. The single centre design and points raised above concerning surgeon experience limit generalisability to other centres and surgeons. The anticipated reduction in complications for both primary outcomes is very ambitious and poses a major limitation when interpreting the final results. While surgical complications can never be avoided, a major reduction seemed both clinically meaningful and achievable based on our pre-trial experience with the procedure. Considering these factors, the resources required to perform a surgical RCT and that transplantation is a relatively low-volume surgery, feasibility also played a significant role in the decided sample size. Ultimately superiority was chosen on the belief that robotic assistance should offer major benefits to both patients and the healthcare system if it is to replace open surgery. However, the trial may prove to be underpowered to demonstrate a smaller difference in complication rates. The trial measures several outcomes,

which were chosen to accommodate important aspects of the procedure to both patients and surgeons but we recognise that not adjusting the significance level for the two primary outcomes and analysing them non-hierarchically increases the risk of type I error. They were deemed of equal importance to determine the risk and benefit of both procedures and adjustment may conversely increase the risk of type II error. To minimise the risk of type I error, the secondary outcomes will be adjusted for multiple testing and all results interpreted in the light of these risks.

The lack of blinding may introduce bias, relating to both patients, personnel and outcome assessors. Medical personnel may make treatment decisions based on perceived benefits and risks related to one of the interventions. Likewise, patients may expect one intervention, particularly robotic surgery, to be superior to the other. Our centre has experienced a blinding surgical approach in trials but given the acute nature of some of the procedures in kidney transplantation, and uncertain benefits, it was deemed impossible and futile [39, 40]. Assessment of the outcomes requires both surgical understanding and review of the EHR and many factors in the EHR ultimately reveal the surgical approach. The multidisciplinary nature of the procedure and the fact that Rigshospitalet is a tertiary centre that treats patients from several peripheral hospitals would require all personnel (both at Rigshospitalet and peripheral hospitals), who come in contact with the patients, even after discharge, to be aware of the required blinding rendering true blinding impossible.

Further risks of bias include subjective assessment of outcomes. While the Clavien-Dindo classification allows for objective assessment of surgical complications as an outcome and has been validated in urology, it does not completely eliminate assessor subjectivity [41]. Likewise, outcomes such as symptomatic haematomas may be open to some degree of interpretation. We sought to minimise these potential risks of bias by pre-defining procedure-specific complications, ensuring all assessors were familiar with the Clavien-Dindo taxonomy and including multiple assessors for any cases of doubt.

Finally, the single components of the composite outcomes may not be of equal consequence to patients such as reoperation vs. death (grade 3 complication vs. grade 5 complication) or symptomatic haematomas vs. vascular thrombosis and a patient may experience several components of the outcome. This requires caution when interpreting results and may limit comparison to other future trials. To account for this and help guide clinicians, the singular complication rates will be made available. In the process of implementing robot-assisted surgery, it is necessary to remain critical about which patients and which parameters robot-assisted surgery might perform better than open surgery.

Ultimately patients should benefit from the implementation of RAKT and this study will contribute with valuable evidence on the possible benefits for both the post-operative and long-term patient trajectory.

Trial status

The protocol is version 1.2 of November 21st, 2023. The trial was initiated in May of 2023 and recruitment is expected to be complete in October of 2025. Enrolment is active at the time of submission.

Abbreviations

DAOH	Days alive and out of hospital
DGF	Delayed graft function
EHR	Electronic health record
LOS	Length of stay
OKT	Open kidney transplantation
PI	Primary investigator
QOL	Quality of life
RAKT	Robot-assisted kidney transplantation
RCT	Randomised clinical trial
REDCap	Research Electronic Data Capture software
SSI	Surgical site infection
UTI	Urinary tract infection

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13063-024-08706-5.

Additional file 1. Definitions of procedure specific complications (Additional file 1.pdf).

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Authors' contributions {31b}

MO serves as the coordinating investigator and trial physician. She has contributed to the study design; developed and drafted the protocol; written all participant information; created the REDCap database; obtained informed consent and handled data collection and monitoring. AR is the principal investigator and sponsor. He has led both the proposal and protocol development and applied for ethical approval from The Committees on Health Research Ethics in the Capital Region of Denmark. JDH conceived the study; contributed to its design; and helped write and develop the protocol. SSS is the co-investigator. He has contributed to the study design and the clinical aspects of protocol development and coordinates the communication between departments of nephrology and urology in collaboration with MR. MR contributed to the clinical aspects of protocol development and coordinated the communication and cooperation between the departments of urology, nephrology and anaesthesiology. TK contributed to the clinical aspects of protocol development and coordinated the cooperation between the departments of urology and anaesthesiology in collaboration with MR. HS contributed to the study design and the statistical aspects of the protocol development. MO drafted the manuscript, AR contributed to writing and all authors read and approved the final manuscript.

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Data availability {29}
After study completion and publication, the trial dataset can be delivered upon reasonable request by contacting the PI or the corresponding author. Access to participant-level data (in a de-identified form) requires approval from the Danish Data Protection Agency.

Declarations

Ethics approval and consent to participate {24}
The trial is approved by The Committees on Health Research Ethics in the Capital Region of Denmark (journal number: H-22065569) and the Danish Data Protection Agency (journal number: P-2022-834). All participants give written, informed consent to participate before randomisation.

Consent for publication {32}
N/A: The consent form includes permission to publish trial data in an anonymised form.

Competing interests {28}
The authors declare they have no competing interests

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References

1. Liem YS, Bosch JL, Arends LR, Heijenbrok-Kal MH, Hunink MGM. Quality of life assessed with the medical outcomes study short form 36-item health survey of patients on renal replacement therapy: A systematic review and meta-analysis. Value in Health. 2007;10(5):390–7.
2. Khandoga A, Thomas M, Kleespies A, Kühnke L, Andrassy J, Habicht A, et al. Surgical complications and cardiovascular comorbidity – Substantial non-immunological confounders of survival after living donor kidney transplantation. Surgeon. 2019;17(2):63–72.
3. Fechner G, Pezold C, Hauser S, Gerhardt T, Müller SC. Kidney's Nightshift, Kidney's Nightmare? Comparison of Daylight and Nighttime Kidney Transplantation: Impact on Complications and Graft Survival. Transplant Proc. 2008;40(5):1341–4.
4. Acedillo RR, Shah M, Devereaux PJ, Li L, Iansavichus AV, Walsh M, et al. The risk of perioperative bleeding in patients with chronic kidney disease: A systematic review and meta-analysis. Ann Surg. 2013;258(6):901–13.
5. Pillot P, Bardonnaud N, Lillaz J, Delorme G, Chabannes E, Bernardini S, et al. Risk factors for surgical complications after renal transplantation and impact on patient and graft survival. Transplant Proc. 2012;44(9):2803–8.
6. Streeter EH, Little DM, Cranston DW, Morris PJ. The urological complications of renal transplantation: A series of 1535 patients. BJU Int. 2002;90(7):627–34.
7. Slagt IKB, IJzermans JNM, Visser Ij, Weimar W, Roodnat JI, Terkivatan T. Independent risk factors for urological complications after deceased donor kidney transplantation. PLoS One. 2014;9(3):1–5.
8. Pillot P, Bardonnaud N, Lillaz J, Delorme G, Chabannes E, Bernardini S, et al. Risk factors for surgical complications after renal transplantation and impact on patient and graft survival. Transplant Proc. 2012;44(9):2803–8.
9. Hernández D, Rufino M, Armas S, González A, Gutiérrez P, Barbero P, et al. Retrospective analysis of surgical complications following cadaveric kidney transplantation in the modern transplant era. Nephrol Dial Transplant. 2006;21(10):2908–15.
10. Bessede T, Droupy S, Hammoudi Y, Bedretdinova D, Durrbach A, Charpentier B, et al. Surgical prevention and management of vascular complications of kidney transplantation. Transpl Int. 2012Sep;25(9):994–1001.
11. Eufrásio P, Parada B, Moreira P, Nunes P, Bollini S, Figueiredo A, et al. Surgical complications in 2000 renal transplants. Transplant Proc. 2011;43(1):142–4.
12. Groth CG, Brent LB, Calne RY, Dausset JB, Good RA, Murray JE, et al. Historic landmarks in clinical transplantation: Conclusions from the consensus conference at the University of California. Los Angeles World J Surg. 2000;24(7):834–43.
13. Hatzinger M, Stastny M, Grützmacher P, Sohn M. The history of kidney transplantation. Urologe A. 2016Oct 12;55(10):1353–9.
14. Kälble T, Lucan M, Nicita G, Sells R, Revilla FJB, Wiesel M. Eau guidelines on renal transplantation. Eur Urol. 2005;47(2):156–66.
15. Basiri A, de la Rosette JJ, Tabatabaei S, Woo HH, Laguna MP, Shemshaki H. Comparison of retropubic, laparoscopic and robotic radical prostatectomy: who is the winner? World J Urol. Springer Berlin Heidelberg. 2018;36(4):609–21.
16. Azawi NH, Rohrsted M, Poulsen J, Lund L, Kromann-Andersen B, Olsen LH. Robotic versus laparoscopic urological surgery: incidence of reoperation and complications. Scand J Urol. 2019;53(1):56–61.
17. Territo A, Gausa L, Alcaraz A, Musquera M, Doumerc N, Decaestecker K, et al. European experience of robot-assisted kidney transplantation: minimum of 1-year follow-up. BJU Int. 2018;122(2):255–62.
18. Giulianotti P, Gorodner V, Sbrana F, Tzvetanov I, Jeon H, Bianco F, et al. Robotic transabdominal kidney transplantation in a morbidly obese patient. Am J Transplant. 2010;10(6):1478–82.
19. Slagter JS, Outmani L, Tran KTCK, Ijzermans JNM, Minnee RC. Robot-assisted kidney transplantation as a minimally invasive approach for kidney transplant recipients: A systematic review and meta-analyses. Int J Surgery Elsevier Ltd. 2022;99:106264.
20. Chapman JR. The KDIGO clinical practice guidelines for the care of kidney transplant recipients. Transplantation. 2010;89(6):644–5.
21. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: A new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surgery. 2004;240:205–13.
22. Maibom SL, Røder MA, Poulsen AM, Thind PO, Salling ML, Salling LN, et al. Morbidity and days alive and out of hospital within 90 days following radical cystectomy for bladder cancer. Eur Urol Open Sci. 2021;1(28):1–8.
23. Roufosse C, Simmonds N, Clahsen-van Groningen M, Haas M, Henriksen KJ, Horsfield C, et al. A 2018 reference guide to the Banff classification of renal Allograft pathology. Transplantation. 2018;102(11):1795–814.
24. Neville A, Lee L, Antonescu I, Mayo NE, Vassiliou MC, Fried GM, et al. Systematic review of outcomes used to evaluate enhanced recovery after surgery. Br J Surg. 2014;101(3):159–71.
25. Wang Y, Hemmelder MH, Bos WJW, Snoep JD, De Vries APJ, Dekker FW, et al. Mapping health-related quality of life after kidney transplantation by group comparisons: A systematic review. Nephrol Dial Transplant. 2021;36(12):2327–39.
26. Redfield RR, Scalea JR, Zens TJ, Muth B, Kaufman DB, Djamali A, et al. Predictors and outcomes of delayed graft function after living-donor kidney transplantation. Transpl Int. 2016;29(1):81–7.
27. Pillot P, Bardonnaud N, Lillaz J, Delorme G, Chabannes E, Bernardini S, et al. Risk factors for surgical complications after renal transplantation and impact on patient and graft survival. Transplant Proc. 2012;44(9):2803–8.
28. Halskov ACL, Dagnæs-Hansen J, Stroomberg HV, Sørensen SS, Røder A. Incidence of and risk factors for recurrent urinary tract infections in renal transplant recipients. Eur Urol Open Sci. 2023;52:115–22.

29. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40(5):373–83.
30. Dagnæs-Hansen J, Kristensen GH, Stroomberg H V, Rohrsted M, Sørensen SS, Røder A. surgical complications following renal transplantation in a large Institutional Cohort. Transplant Direct. 2024;10(6):e1626. Available from: https://journals.lww.com/10.1097/TXD.0000000000001626.
31. Fergusson D, Aaron SD, Guyatt G, Hébert P. Post-randomisation exclusions: The intention to treat principle and excluding patients from analysis. Br Med J. 2002;325(7365):652–4.
32. Moretto S, Gandi C, Bientinesi R, Totaro A, Marino F, Gavi F, et al. Robotic versus open pyeloplasty: perioperative and functional outcomes. J Clin Med. 2023;12(7):2538.
33. Martin RCG, Brennan MF, Jaques DP. Quality of complication reporting in the surgical literature. Ann Surg. 2002;235(6):803–13.
34. Ghaferi AA, Dimick JB. Considering surgeon skill in randomized clinical trials. JAMA Surg. 2020;155(7):599.
35. Robinson NB, Fremes S, Hameed I, Rahouma M, Weidenmann V, Demetres M, et al. Characteristics of randomized clinical trials in surgery from 2008 to 2020: a systematic review. JAMA Netw Open. 2021;4(6):1–13.
36. Birkmeyer JD, Stukel TA, Siewers AE, Goodney PP, Wennberg DE, Lucas FL. Surgeon volume and operative mortality in the United States. N Engl J Med. 2003;349(22):2117–27.
37. Sood A, Ghani KR, Ahlawat R, Modi P, Abaza R, Jeong W, et al. Application of the statistical process control method for prospective patient safety monitoring during the learning phase: Robotic kidney transplantation with regional hypothermia (ideal phase 2a-b). Eur Urol. 2014;66(2):371–8.
38. Outmani L, IJzermans JNM, Minnee RC. Surgical learning curve in kidney transplantation: A systematic review and meta-analysis. Transpl Rev. WB Saunders. 2020;34(4):100564.
39. Maibom SL, Røder MA, Aasvang EK, Rohrsted M, Thind PO, Bagi P, et al. Open vs robot-assisted radical cystectomy (BORARC): a double-blinded, randomised feasibility study. BJU In. 2022;130(1):102–13. Available from: https://bjui-journals.onlinelibrary.wiley.com/doi/10.1111/bju.15619.
40. Catto JWF, Khetrapal P, Ricciardi F, Ambler G, Williams NR, Al-Hammouri T, et al. Effect of robot-assisted radical cystectomy with intracorporeal urinary diversion vs open radical cystectomy on 90-day morbidity and mortality among patients with bladder cancer: a randomized clinical trial. JAMA - Journal of the American Medical Association. 2022;327(21):2092–103.
41. Mitropoulos D, Artibani W, Biyani CS, Bjerggaard Jensen J, Rouprêt M, Truss M. Validation of the Clavien–Dindo grading system in Urology by the European Association of Urology Guidelines Ad Hoc Panel. Eur Urol Focus. 2018;4(4):608–13. Available from: https://linkinghub.elsevier.com/retrieve/pii/S2405456917300627.

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