Fasting before live kidney donation, effect on donor wellbeing and postoperative recovery

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The primary objective is to determine the effect of nutritional preconditioning by fasting with a lowdose laxative on the severity of postoperative fatigue at 4 weeks after donor nephrectomy in adult patients.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON55223

Source
ToetsingOnline

Brief title
FAST-Study

Condition

- Other condition
- Renal disorders (excl nephropathies)
- Renal and urinary tract therapeutic procedures

Synonym
Postoperative fatigue / DNA-Damage / Ischemia-reperfusion Injury / after live kidney donation

Health condition

Upregulatie van beschermende cytokinen tegen oxidatieve schade tgv dieetrestrictie

Research involving

Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Fasting, Living Kidney donation, Postoperative fatigue, Postoperative recovery

Outcome measures

Primary outcome

Postoperative fatigue, scored by 36-Item Short Form Health Survey (RAND-36).

The primary endpoint will be measured 4 weeks after surgery.

Secondary outcome

Postoperative fatigue, measured by QoR-40, scored 4 weeks after surgery.

Postoperative hospital admission time, measured in days since surgery.

Adherence to the fasting regime

- Self-reported adherence

- Change of body weight

- Blood samples on the day of surgery

Physical activity before, during and after hospital stay

- Determined by SmartWatches, 1 week prior and 2 weeks after surgery.

Postoperative recovery of renal function in the donor

- Change in Creatinine, Cystatine C, Urea, protein content in urine, and renal function (eGFR by Cockcroft/CKD-EPI)

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Postoperative recovery of renal function in the transplanted patient

- Change in Creatinine, Cystatine C, Urea, protein content in urine, and renal function (eGFR by Cockcroft/CKD-EPI)

- Incidence of delayed graft function (defined as the need of dialysis in 1 week after transplantation)

- Incidence of acute rejection, biopsy proven

Determination of upregulation of cytoprotective genes / anti-inflammatory markers

- Lab testing, blood samples drawn on day 0

- Kidney biopsy, acquired after donation and after reperfusion

- Tissue retrieval of distal ureter and peri-renal fat

Investigate the use and merit of uEV in renal transplantation in human subjects and the effect of fasting on uEV

- Assess the change in uEV between fasted en non-fasted subjects

- Assess the correlation between uEV, histopathological changes and postoperative renal function

- Investigate the use of urinary extracellular vesicles as a predictive biomarker of future graft function

To assess the effect of fasting on immune cells in the blood (e.g. higher/lower quantity of immune cells, more/less activation,maturation or differentiation of those cells)

Study if the immune-modulating effect of fasting correlates with post-operative recovery of kidney donors.

Study description

Background summary

Enhanced Recovery After Surgery (ERAS) reduces both hospital stay and complication rates. Part of the ERAS protocol consist of early postoperative mobilization and ad libitum diet. However, no clear recommendation of a preoperative diet has been made. Further research should be conducted to improve the recovery time and lessen postoperative fatigue, one of the main postoperative effectors on donor quality of life (QoL).

Dietary restriction (DR and intermittent fasting are associated with extended life span, lower risk of age associated diseases, improved fitness and increased resistance to acute stress. DR and fasting represent non-invasive, non-expensive methods of mitigating the effects of acute surgery-induced stress. Short-term dietary restriction and fasting increases expression of cytoprotective genes, increases immunomodulation via increased anti-inflammatory cytokine production and also decreases the expression of pro-inflammatory markers. DR has been proven feasible and safe in well-nourished patients before live kidney donation. A recent study shows the beneficial effect of DR on disease control of acromegaly patients.

Dietary restriction can be performed in different regimens. For long term DR subjects can reduce their daily energy intake with 30% for several weeks or longer. Another regimen is a short water-only fasting, triggering the same protective effect . The use of laxatives might affect the timing of the protective effect of fasting. Live kidney donors are an excellent study population to further investigate the beneficial effect of preoperative preconditioning by fasting. Recent studies proved the feasibility of short-term DR and its merits. To investigate whether the beneficial effect of preoperative fasting reduces the postoperative fatigue after live kidney donation, a larger randomized clinical trial is needed. This research is needed since postoperative fatigue is one of the main effectors on donor quality of life

(QoL).

Study objective

The primary objective is to determine the effect of nutritional preconditioning by fasting with a lowdose laxative on the severity of postoperative fatigue at 4 weeks after donor nephrectomy in adult patients.

Study design

a multicenter randomized controlled trial.
- Group 1: Control group, no change in diet.
- Group 2: Intervention group: preoperative fasting for 2,5 days and low dose laxatives once daily

Intervention

Preoperative nutritional preconditioning by a 2,5 day fast, with the use of a low dose laxatives.

60 hours before surgery (2,5 days), subjects start a fasting regime. Fasting is defined as no caloric intake. Subjects are free to drink unlimited water, tea and coffee (without sugar or milk) to maintain a sufficient fluid balance. In addition, they are allowed a daily dose of 100 grams of vegetables (cucumber, baby carrots and baby tomatoes). To prevent the loss of electrolytes they are allowed 3 *Drinkbouillon* (Knorr Tuinkruiden: 3,6 grams per cup, containing 4kcals) or *Opkikkertjes* (Maggi: 3,3 grams per cup , containing 7 kcals). After surgery, the subjects are free to eat what and how much they want.

Participants in the intervention group also use 1 dose of Macrogol 3350 (13,1 grams and electrolytes) each day for 3 days before surgery.

Study burden and risks

The extent of the burden of our study is considered relatively low. Dietary restriction has been proven feasible and safe in previous studies. For this study, extra blood samples are taken at a regular invasive procedure, besides the samples taken for routine procedures. If a patient takes part in the additional substudy, additional blood samples will be taken. A maximum of 2 additional venous punctures are necessary. A maximum of one extra visit to the hospital is needed in order to obtain all the information required for this study. Peri-operatively, biopsies of the kidney are also taken. The perioperative biopsies have been shown to carry no to very little risk. Several standardized questionnaires are asked to be filled in before, during and after the diet. Mentioned questionnaires take 2-10 minutes to complete. The diet may give rise to discomfort in the form of less satiety and possible

light-headedness. No other risks concerning the dietary intervention is to be expected.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Adult patients and donors opting for living kidney donation and transplantation at Erasmus MC, University Medical Center in Rotterdam, the Netherlands and University Medical Center Groningen in Groningen, the Netherlands

In order to be eligible to participate in this study, a subject going for live kidney donation must meet all of the following criteria:
- Age between 18 and 70 years old
- BMI between 19 and 35 kg/m2

- Provide written consent
- Adequate understanding of the Dutch language

Exclusion criteria

A potential subject (Donor) who meets any of the following criteria will be excluded from participation in this study:
- Participants of the cross-over kidney donation program
- Participation in another prospective trial/study for live kidney donors
- HLA- or bloodtype-incompatible living kidney donation

A potential subject (Recipient) who meets any of the following criteria will be excluded from participation in this study:
- the use of double anticoagulants (f.i. Ascal (Carbasalate Calcium) and Clopidogrel (Plavix)).
- the need for therapeutic anticoagulation with low-molecular weight heparine during admission for kidney transplantation, also known as *Bridging*.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	26-05-2021
Enrollment:	180
Type:	Actual

Medical products/devices used

Registration:	No

Product type:	Medicine
Brand name:	Compound Macrogol Oral Powder Sugar Free.
Generic name:	Macrogol 3350
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	18-02-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-02-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	14-09-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-11-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-08-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2020-005445-16-NL
CCMO	NL74623.078.21