Trial Description

Title

Remote Ischemic Preconditioning (RIPC) versus sham-control for reduction of Anastomotic Leakage after resection for rectal cancer: a prospective, randomized controlled, triple-blind, clinical phase III monocenter trial

Trial Acronym

RIPAL

URL of the trial

http://no website available

Brief Summary in Lay Language

Anastomotic leakage (= suture leaking) is a dreaded complication after surgery on the rectum. This often occurs due to ischemia (= reduced blood supply) of the anastomotic region. There is still an urgent need for methods to prevent suture leaks, which can be devastating, causing septicemia, reoperation, or even the death of the patient. "Remote ischemic preconditioning" (RIPC) is a novel approach in which a short amount of hypoperfusion is given away from the target organ (e.g., intestine or liver) e.g. by inflating a blood pressure cuff on an arm for 5 minutes. As a result, bodily substances, which mediate a complex control loop that protects against damage from reduced blood flow to the target organ. Numerous studies have demonstrated this protective effect for RIPC in various organs (e.g., brain, heart, kidney, liver). The planned study is the first study and the first pilot RCT (randomized controlled trial) that will investigate whether RIPC reduces the rate of anastomotic leakage after resection for rectal cancer compared to the control intervention (= sham-RIPC). During the 30-day follow-up period, the following outcomes will be assessed: surgical complications, reinterventions, hospital stay, readmission. A positive study outcome would be of high patient and clinical relevance due to the serious effects of anastomotic leakage.

Brief Summary in Scientific Language

"Remote ischemic preconditioning" (RIPC) is an innovative approach that differs from other preconditioning strategies in that the ischemic stimulus (by inflating a blood pressure cuff on one extremity) is performed remotely from the target organ. As a result, several cytokines, are released, which protect the target organ against ischemic damage via a complex control loop. RIPC induces the release of serotonin from platelets, which stimulates VEGF secretion, which in turn up-regulates the release of IL10 and Mmp8 in the target organs. There are already multiple studies demonstrating that RIPC attenuates ischemia-reperfusion injury in various organ systems.
Gastrointestinal anastomoses are highly vulnerable to ischemic injury and therefore anastomotic leakage has often an ischemic genesis. To what extent RIPC after rectal resection has a protective effect on the development of anastomotic leakage is still unclear.

Do you plan to share individual participant data with other researchers?

No

Description IPD sharing plan

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Organizational Data

- DRKS-ID: **DRKS00018942**
- Date of Registration in DRKS: **2019/10/31**
- Date of Registration in Partner Registry or other Primary Registry: **[---]***
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **2019-730N , Medizinische Ethik-Kommission II Medizinische Fakultät Mannheim der Universität Heidelberg**

Secondary IDs

Health condition or Problem studied

- ICD10: **C20 - Malignant neoplasm of rectum**
- ICD10: **K91.83 - [generalization K91.8: Other postprocedural disorders of digestive system, not elsewhere classified]**

Interventions/Observational Groups

- Arm 1: **Experimental Arm/ Study Intervention: In RIPC, a blood pressure cuff is placed around an arm immediately prior to surgery (after induction of anesthesia and before/ during incision/dissection) and inflated to 200 mmHg or a pressure ≥50 mmHg above systolic pressure for 5 minutes (= limb ischemia). This corresponds to the ischemic stimulus distant from the target organ and is followed by a 5-min break (= limb reperfusion). The whole schedule is performed three times for a total of three 10-min cycles (= 30 min/patient).**
- Arm 2: **Control Arm/ "sham"-RIPC: In "sham"-RIPC, a blood pressure cuff is placed around an arm immediately prior to surgery (after induction of anesthesia and before/ during incision/dissection), but NOT inflated. This is followed by a 5-min break. The whole schedule is performed three times for a total of three 10-min cycles (= 30 min/patient).**

Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***
- Allocation: **Randomized controlled trial**
- Blinding: **[---]***
- Who is blinded: **patient/subject, investigator/therapist, assessor, data analyst**
- Control: **Placebo**
- Purpose: **Prevention**
- Assignment: **Parallel**
- Phase: **III**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **N/A**

Primary Outcome

The primary endpoint is the anastomotic leakage rate within 30 days after surgery. Anastomotic leakage is defined and classified according to the recommendation of the International Study Group of Rectal Cancer (Rahbari NN et al. (2010) Definition and Grading of Anastomotic Leakage: a proposal by the International Study Group of Rectal Cancer Surgery 147 (3): 339-351). In patients with suspicious clinical symptoms (pain, fever, increased infection parameters, tachycardia / hypotension), anastomotic leakage is confirmed / excluded by endoscopic or radiographic (computed tomography with rectal contrast enema) examinations. This corresponds to the clinical standard. All asymptomatic patients will undergo an endoscopic control of anastomotic healing on postoperative day (POD) 5 (+/- 1 day) to assess the primary endpoint.

Secondary Outcome

Secondary endpoints are perioperative morbidity and mortality (Clavien-Dindo classification), conduit necrosis, chyle leak, recurrent nerve palsy (defined by the ECCG), need for/duration of re-interventions (endoluminal vacuum therapy, interventional drainage, re-operation), hospital/ICU stay and readmissions. Effects of RIPC on biomarkers of ischemia-reperfusion injury (serotonin, VEGF) and necrotic cell death (Hmgb1) will be measured in plasma before RIPC (t0), immediately after RIPC (t1), and at 3 hours after RIPC (t2) using ELISA.

Countries of recruitment

- DE **Germany**

Locations of Recruitment

- University Medical Center **Chirurgische Klinik, Mannheim**

Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2019/12/10**
- Target Sample Size: **56**
- Monocenter/Multicenter trial: **Monocenter trial**
- National/International: **National**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **no maximum age**

Additional Inclusion Criteria

Persons meeting the following criteria may be included in the study:
• Planned elective continence-preserving rectal resection for rectal cancer
• Signed informed consent
• Age ≥18 years

Exclusion criteria

Persons meeting any of the following criteria cannot be included in the study:
• Patients not able to give informed consent
• Patients presenting with the following contraindications to the study intervention (RIPC): arterial occlusive disease (AOD), infections or wounds on the upper extremity, poorly controlled diabetes mellitus, or deep vein thrombosis of the upper extremity

Addresses

- **Primary Sponsor**

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- **Contact for Scientific Queries**

Contact for Scientific Queries

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Sources of Monetary or Material Support

- **Institutional budget, no external funding (budget of sponsor/PI)**

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Status

- Recruitment Status: **Recruiting ongoing**
- Study Closing (LPLV): **[---]***

Trial Publications, Results and other documents

Deutsches Register Klinischer Studien
German Clinical Trials Register

* *This entry means the parameter is not applicable or has not been set.*
*** *This entry means that data is not displayed due to insufficient data privacy clearing.*