Low impact laparoscopy (low pressure pneumoperitoneum and deep neuromuscular blockade) versus standard laparoscopy during robot assisted radical prostatectomy to improve the quality of recovery and immune homeostasis; a randomized controlled study.

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- To establish the relationship between the use of deep neuromuscular blockade (NMB) with low pressure pneumoperitoneum (PNP) and the quality of recovery after RARP.- To establish the relationship between the use of deep neuromuscular blockade (NMB...

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

Summary

ID

NL-OMON49113

Source
ToetsingOnline

Brief title
RECOVER 2

Condition

- Other condition

Synonym
Postoperative recovery and immune homeostasis

Health condition

postoperatief herstel en effect op immuunsysteem na robotgeassisteerd laparoscopische ingrepen.

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: merck

Intervention

Keyword: Neuromuscular block, pneumoperitoneum, Robotassisted laparoscopy

Outcome measures

Primary outcome

- Quality of recovery score (QoR-40) at postoperative day 1.

- IL-6 and IL-10 response upon whole blood LPS stimulation at postoperative day

7.

- Perfusion index of the parietal peritoneum as calculated from the slope of

ICG fluorescence intensity, and time to maximal intensity in seconds.

(extracted from video registration).

Secondary outcome

QoR-40 score (day 1 and day 10-12), SF-36 score (1 day before, 10-12 days and 3

months after surgery), McGill pain questionnaire (3 months after surgery), pain

scores, analgesia use, PONV, time to reach discharge criteria, length of

hospital stay, surgical conditions and postoperative complications scored by

Clavien Dindo classification.

Study description

Background summary

Intra-abdominal pressure (IAP) needed to create sufficient workspace during laparoscopic surgery affects the surrounding organs with ischemia-reperfusion injury and a systemic immune response. This effect is related to postoperative recovery, pain scores, opioid consumption, bowel function recovery, morbidity and possibly mortality. In clinical practice standard pressures of 12-16mmHg are applied instead of the lowest possible IAP, but accumulating evidence shows lower pressure pneumoperitoneum (PNP) (6-8mmHg) to be non-compromising for sufficient workspace, when combined with deep neuromuscular blockade (NMB) in a vast majority of patients. Therefore, low impact laparoscopy, meaning low pressure PNP facilitated by deep NMB, could be a valuable addition to Enhanced Recovery After Surgery (ERAS) Protocols.
Increased IAP can cause peritoneal mesothelial injury either directly or by compression of small vessels including capillaries, leading to a variable degree of ischemia reperfusion injury. The compromised perfusion of the parietal peritoneum can be visualized and quantified by a fluorescent marker such as Indocyanine green (ICG), as shown in a previous pilot study. Hypoxic injury of intra-abdominal organs and/or tissues may cause the release of Danger Associated Molecular Patterns (DAMPs). It is known that after trauma and sepsis, the release of DAMPs is associated with immunoparalysis and a higher susceptibility to infectious complications. The use of low pressure PNP may reduce hypoxic injury and the release of DAMPs and thereby contributing to a better preservation of innate immune function which may help to reduce the risk of infectious complications.

Study objective

- To establish the relationship between the use of deep neuromuscular blockade (NMB) with low pressure pneumoperitoneum (PNP) and the quality of recovery after RARP.
- To establish the relationship between the use of deep neuromuscular blockade (NMB) with low pressure pneumoperitoneum (PNP) and innate immune function after RARP.
Secondary objectives:
- To study whether low pressure PNP and/or deep NMB affects the perfusion of the parietal peritoneal layer during RARP.

Study design

A mono-center, randomized controlled clinical trial.

Intervention

The participants will be randomly assigned in a 1:1 fashion to:
- Experimental group: low impact laparoscopy (low pressure (8 mmHg) and deep NMB (PTC 1-2))
- Control group: standard laparoscopy (standard pressure (14 mmHg) and moderate NMB (TOF 1-2))
At the start of surgery, after intra-abdominal insufflation, ICG injection will take place with starting pressure to quantify parietal peritoneum perfusion, and a parietal peritoneal biopsy will be taken. At the end of surgery, a second parietal peritoneum biopsy will be taken.

Study burden and risks

The use of a deep NMB enables the safe use of low-pressure PNP. If despite a deep NMB visibility is compromised, pressure will be increased to minimize surgery related risks. A deep NMB is achieved by higher doses of rocuronium which are within normal therapeutic range used in clinical practice, and is safe to use. Depth of NMB will be monitored throughout the whole surgery. At the end of surgery, the effects of rocuronium will be antagonized by sugammadex to avoid residual paralysis. Indocyanine green is a registered product routinely used to quantify tissue perfusion during this surgery. The total dose during surgery is below the advised maximum dose of 5 mg/kg. Any possible risk factors or interactions as mentioned in the Summary of Product Characteristics are covered by exclusion criteria in order to fully eliminate risk of participation. Regarding the peritoneal biopsies; peritoneal tissue is directly visible and easily accessible during laparoscopic surgery and biopsies are obtained in a standardized manner with hemostasis when needed under direct vision. Therefore, no additional complications are expected. Blood samples will be combined with routine laboratory assessment where possible. Previous studies have shown low-pressure PNP is associated with reduced postoperative pain scores, reduced opioid consumption and improved bowel function. This may lead to enhanced recovery. The burden for participants is mainly related to the evaluation of the endpoints during the early postoperative phase. Assessment of pain scores, nausea, complications and discharge criteria are part of the normal treatment. Questionnaires will take approximately 10-15 minutes per time-point.

Contacts

Public
Radboud Universitair Medisch Centrum

Geert grooteplein 10
Oss 6500HB
NL
Scientific
Radboud Universitair Medisch Centrum

Geert grooteplein 10
Oss 6500HB
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Age * 18 years
- Undergoing elective robot assisted radical prostatectomy (RARP)
- Obtained informed consent

Exclusion criteria

- Laparoscopic radical prostatectomy without robot assistance
- Insufficient control of the Dutch language to read the patient information and to fill out de questionnaires
- Neo-adjuvant chemotherapy
- Chronic use of analgesics or psychotropic drugs
- Use of NSAID*s shorter than 5 days before surgery
- Severe liver- or renal disease
- Neuromuscular disease
- Hyperthyroidism or thyroid adenomas
- Deficiency of vitamin K dependent clotting factors or coagulopathy
- Planned diagnostics or treatment with radioactive iodine < 1 week after

surgery
- Indication for rapid sequence induction
- BMI >35kg/m2
- Known of suspected hypersensitivity to ICG, sodium iodide, iodine, rocuronium or sugammadex
- Use of medication interfering with ICG absorption as listed in the summary of product characteristics (SPC); anticonvulsants, bisulphite compounds, haloperidol, heroin, meperidine, metamizol, methadone, morphium, nitrofurantoin, opium alkaloids, phenobarbital, phenylbutazone, cyclopropane, probencid.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	13-12-2020
Enrollment:	96
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Bridion
Generic name:	sugammadex
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Rocuronium

Generic name:	Rocuronium
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	26-05-2020
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2020-000411-79-NL
CCMO	NL72780.091.20