A step-up approach: CRP first followed by CT-scan imaging to ensure Quality Control after Major Abdominal Surgery. the PRECious trial

Published: 26-05-2015
Last updated: 15-04-2024

Aim of the PRECious trial is to evaluate the effect of a standardized postoperative algorithm for quality control (via standardized measurement of CRP levels and CT-scan imaging) on morbidity and mortality after major digestive surgery.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal therapeutic procedures
Study type	Interventional

Summary

ID

NL-OMON47788

Source
ToetsingOnline

Brief title
PRECious trial

Condition

- Gastrointestinal therapeutic procedures

Synonym
complications which necessitate invasive treatment, major complications

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: CRP, CT, Major Abdominal Surgery, postoperative complications

Outcome measures

Primary outcome

1. Mortality; during 12 month follow-up

2. Morbidity associated with major complications and/or after reoperation

within 12 months after index operation, including:

o Fistula after reoperation; connection between two hollow-organs and/or skin;

entero-cutaneous, entero-vesical and entero-vaginal fistula.

o Wound dehiscence/incisional hernia/open abdomen after reoperation;

full-thickness discontinuity in abdominal wall with bulging of abdominal

contents, with or without obstruction.

o Bowel obstruction or herniation after major complication; Due to adhesions,

diagnosis to be confirmed in CT or surgery.

o Abscess; pus-containing non pre-existent cavity, requiring percutaneous

drainage or surgery. Confirmed by gram-stain or culture.

o Abdominal compartment syndrome after reoperation: intra-abdominal

hypertension > 25 mmHg (modified Burch criteria) with tense abdomen and with

increasing respiratory and/or renal failure. Measured by the urinary bladder

pressure method.

o Perforation of visceral organ after major complication and confirmed at

surgery

o Unplanned enterostomy upon reoperation

o Enterostomy dysfunction due to prolapse, stenosis or retraction.

o Myocardial infarction: electrocardiogram and enzyme changes suggestive of myocardial infarction and/or admission to coronary care unit

o Pulmonary embolus; confirmed on ventilation perfusion scan or CTa-scan

o Respiratory insufficiency due to pneumonia, pleural effusion or pulmonary edema; necessitating mechanical ventilation.

o Cerebrovascular accident; ischemic or non-ischemic with persistent paresis or paralysis without previous history

o Renal failure; urine production<500 ml/24h with rising levels of blood urea nitrogen and creatinin, combined with dehydration; necessitating any form of dialysis

o Urosepsis; urinary tract infection with positive urine and blood cultures and circulatory shock.

o Upper GI bleeding requiring endoscopic treatment or embolization therapy

o Intra-abdominal bleeding; surgical bleeding after relaparotomy or hematoma requiring surgical evacuation.

o Anastomotic leak after relaparotomy requiring precutaneous drainage or reoperation

Secondary outcome

Secondary outcome measures are:

* Quality of Life as measured by; EQ-5D 5L Questionnaire

* Add-on value of CRP (only measured during intervention period): Grading of

patient by physician in charge during morning visits, before CRP levels are measured, on a scale of 0 -10 (zero being healthy patient, ten being a patient at risk of acute death).

* Duration of admission

* Duration of intensive care admission

* Cost-efficiency

Study description

Background summary

In major digestive surgery, defined als all gastrointestinal resections with reconstruction via anastomosis or ostomy, major postoperative complications are observed in up to 20% of patients. These complications necessitate invasive treatment such as reoperation, percutaneous drainage and intensive care admission and are associated with increased morbidity and mortality, which in turn leads to longer lengths of hospital and intensive care stay, unplanned procedures, increased risk of cancer recurrence and higher costs.
Current time to diagnosis of major complications is approximately 8 days. A delay in diagnosis is associated with a further increase in morbidity and mortality. Early diagnosis and treatment decreases morbidity and mortality, but is challenging since with clinical, serological and even imaging techniques the difference between a complications and physiological postoperative response can be hard to distinguish. Furthermore, clinical assessment showed a low predictive value for anastomotic leakage. This further supports the need for a standardized quality control algorithm after major abdominal surgery. At the moment no such standardized algorithm exists.

C-reactive protein (CRP) is a known marker of infection and inflammation. This acute phase protein is synthesized in the liver after stimulation by cytokines. CRP is elevated after surgery. a peak is observed 48-72 hours postoperatively. Half-life of CRP is approximately 19 hours and independent of diet, diurnal rhythm and organ function. Due to these characteristics CRP is considered a valuable marker for inflammation.
Several studies have assessed the use of CRP as a marker for postoperative complications, with promising results. Based on our own systematic review and pooled-analysis of 1427 patients we established an optimal cut-off of 140 mg/L on postoperative day 3,4 and 5, with a sensitivity of 81,7% and specificity of 61,6%.

CRP is however non-specific for location, thus additional imaging is required. Computed Tomography scan imaging (CT-scan) is the current imaging modality of choice. In our database of 399 patients CT-scan imaging showed a sensitivity of 91,7% and specificity of 100% for diagnosis of major complications, this is confirmed in recent literature.

In 2008 Den Dulk et al. implemented a standardized scoring system for the clinical status of patients after colorectal surgery. With this system they managed to decrease the time between index operation and diagnosis of anastomotic leakage from 8 to 6 days. Furthermore, mortality decreased from 39% to 24% (p=0,24). This study further supports the need for a standardized quality control algorithm after major digestive surgery, however the optimal algorithm is yet to be established. CRP and CT-scan imaging adequately aid diagnosis of postoperative complications, however currently their use is only on demand. The PRECious protocol is a standardized postoperative algorithm aimed at quality control and early diagnosis and treatment of major complications.

Study objective

Aim of the PRECious trial is to evaluate the effect of a standardized postoperative algorithm for quality control (via standardized measurement of CRP levels and CT-scan imaging) on morbidity and mortality after major digestive surgery.

Study design

The PRECious trial is performed based on a stepped-wedge design, it is a multi-center study. In the first phase of the trial all patients will be allocated to the control group (n=350). These patients receive standard postoperative care and standard CRP measurements on postoparative day 3,4 and 5, for observational purposes.
After an implementational phase of one month, all patients will be allocated to the intervention group (n=350). Patients allocated to this group will receive postoperative monitoring according to the PRECious protocol, which entails standardised measurements of CRP on postoperative day 3,4 and 5. If CRP levels exceed 140 mg/L on postoperative day 3,4 or 5, additional CT-scan imaging of the operated area will be performed.

Intervention

Standard postoperative monitoring, which includes only "on demand" additional laboratory testing is compared to the PRECious protocol. The PRECious protocol entails standardized CRP measurements on postoperative day 3,4 and 5. If CRP levels exceed 140 mg/L, additional CT-scan imaging will be performed to

diagnose or exclude major complications.

Study burden and risks

The PRECious trial aims to establish the effect of standardised postoperative quality control on postoperative morbidity and mortality associated with major complications.
Risks and burden associated with participation in the study are believed to be low. In the intervention group patients are subjected to three venous punctures, which can be complicated by formation of a hematoma, dizziness and collaps. These complications are all transient.
If measured CRP levels exceed 140 mg/L additional CT-scan imaging is performed. Risks of CT-scan imaging consist of radiation risks. As stated above, the risks due to radiation are believed to be low and are surpassed by the morbidity and mortality asscoated with delays in diagnosis of complications. Other possible complications are mainly associated with the contrast materials, hence patients with known allergies for contrast are not included in the study. Similarly patients with decreased (GFR < 30 ml/min/1,73 m2) renal function are not included and renal function is monitored in all patients undergoing CT-scan imaging.

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

Patient older than 18 years of age
Patients planned for elective Major Abdominal Surgery
Informed consent

Exclusion criteria

Patients undergoing acute major abdominal surgery
ASA (American Society of Anaesthesiologists) classification of 4 or higher
Insufficient dutch language skills
Contrast allergies
glomerular filtration rate (GFR)of less than 30 ml/min/1,73m2 or patients with multiple myeloma

Study design

Design

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

Primary purpose: Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-11-2015
Enrollment:	700

Type:	Actual

Ethics review

Approved WMO Date:	26-05-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-10-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-09-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-10-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-06-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
ClinicalTrials.gov	NCT02102217
CCMO	NL43534.029.15