Inflammation and complications after pulmonary surgery for cancer

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Primary Objective: - To identify relative IL-6 thresholds (% increase from baseline and % decrease from the peak postoperative value) for predicting infectious complications after pulmonary surgerySecondary Objective(s): - To identify relative IL-6…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON46474

Source
ToetsingOnline

Brief title
ICAPSUC

Condition

- Other condition
- Respiratory tract neoplasms
- Respiratory tract therapeutic procedures

Synonym
complication, complications after lung surgery, postoperative outcome

Health condition

postoperatieve complicaties

Research involving
Human

Sponsors and support

Primary sponsor: Amphia Ziekenhuis
Source(s) of monetary or material Support: Roche

Intervention

Keyword: inflammation, perioperative care, postoperative complications, pulmonary surgical procedures

Outcome measures

Primary outcome

Main study parameters are levels of IL-6, CRP, leucocyte count, PCT, ntproBNP,

GDF-15 and hs-cTn.

Primary endpoint is the development of an infectious complication which is

defined as one of the following outcomes within 30 days of surgery:

- pneumonia (purulent sputum, positive sputum or blood culture and clinical

symptoms such as cough, fever or consolidation on chest radiograph)

- pulmonary empyema (pleural effusion and the presence of pus on pleural

aspiration, microorganism on pleural fluid culture or positive pleural fluid

Gram stain)

- sepsis (qSOFA score >=2 in response to an infection)

- wound infection (purulent drainage from superficial incision or deliberate

opening of superficial incision by surgeon and pain, tenderness, swelling or

redness)

- urinary tract infection (urinary tract symptoms or fever and urine culture

with no more than 2 species of organisms identified with at least one of which

is a bacterium of >=105 CFU/ml)

Secondary outcome

Secondary endpoint is the development of a non-infectious complication which is defined as one of the following outcomes within 30 days of surgery:

- acute kidney injury (increase in serum creatinine by >= 26 µmol/l, a percentage increase in serum creatinine of more than or equal to 50% or oliguria of less than 0.5 ml/kg per hour for more than six hours within 48 hours)
- respiratory insufficiency (hypoxia or hypercapnia leading to ICU (re)admission)
- reoperation
- supraventricular arrhythmia (new-onset atrial fibrillation or atrial flutter)
- congestive heart failure (pleural effusion or pulmonary edema requiring diuretic therapy)
- acute respiratory distress syndrome (defined as diffuse inflammatory lung injury (onset over 1 week or less), bilateral opacities consistent with pulmonary edema must be present and may be detected on CT or chest radiograph, PF ratio <300mmHg with a minimum of 5 cmH20 PEEP (or CPAP) must not be fully explained by cardiac failure or fluid overload
- pulmonary embolus (filling defect >= 75% in a pulmonary artery with corresponding normal ventilation
- stroke (clinical diagnosis of acute transient ischemic attack (TIA) or cerebrovascular accident (CVA))

- myocardial infarction (elevated hs-cTn in combination with clinical symptoms or electrocardiography changes)

- mortality

Other secondary endpoints that will be captured are any complication (which is a composite of infectious and non-infectious complications within 30 days of surgery), length of ICU stay and length of hospital stay.

For both the primary and secondary endpoints the exact time (in hours and days after surgery, and during or after ICU admission) on which the endpoint is reached will be noted.

Study description

Background summary

Up to 50% of patients undergoing pulmonary surgery for cancer suffer from complications such as pneumonia, respiratory insufficiency, cardiac arrhythmia and death. Postoperative complications are a major determinant of survival up to five years after surgery and therefore a potential target to improve surgical outcome.
Currently, the identification of patients at high risk of postoperative complications is often based on levels of proinflammatory biomarkers, such as levels of C-reactive protein (CRP) and leucocyte count. Unfortunately, the specificity and sensitivity for the prediction of complications in the first days following surgery is relatively low. This can be partly explained by the slow change of CRP levels and leucocyte count in response to an inflammatory insult.
Interleukin-6 (IL-6) is a proinflammatory biomarker that is produced by monocytes in response to tissue injury. Levels of IL-6 increase within 60 minutes, peak after 4 to 6 hours and usually return rapidly to baseline due to the short plasma half-life of 2 to 6 hours (compared to 19 hours for CRP). In a recent study, levels of IL-6 on postoperative day 1 had a similar diagnostic accuracy as levels of CRP on postoperative day 3 for the prediction of

complications following major abdominal surgery. This may suggest that introducing IL-6 measurements after surgery may lead to an earlier detection of complications and possibly improved long-term outcome.
Until now, clinicians have focussed on absolute peak levels of proinflammatory biomarkers during the immediate postoperative period. The underlying idea is that inflammation induced by surgical trauma is harmful when the inflammatory response is excessive. However, there is a great variation in levels of proinflammatory biomarkers between patients and peak levels of proinflammatory biomarkers have low diagnostic value for the prediction of postoperative complications. It is possible that changes in levels of inflammatory biomarkers over time have a higher discriminative power for identifying patients at high or low risk of postoperative complications than absolute peak levels. For example, an initial proinflammatory biomarker peak on the first postoperative day followed by a rapid decline to baseline in the following days after surgery may indicate a physiological, innocent inflammatory response, while a sustained elevation points to an increased risk of complications. Given the vivid dynamics and rapid changes over time, levels of IL-6 appear to be the most useful marker to study this hypothesis.

Study objective

Primary Objective:

- To identify relative IL-6 thresholds (% increase from baseline and % decrease from the peak postoperative value) for predicting infectious complications after pulmonary surgery

Secondary Objective(s):

- To identify relative IL-6 thresholds for predicting non-infectious complications and any complication (a composite of infectious and non-infectious complications) after pulmonary surgery
- To compare the prognostic accuracy of relative IL-6 thresholds for predicting infectious, non-infectious and any postoperative complication to other biomarkers as CRP, leucocyte count, procalcitonin (PCT), ntproBNP, GDF-15 and high-sensitive cardiac troponin (hs-cTn)

Study design

Multicentre prospective observational cohort study with a follow up time of 30 days after surgery. Patients will be included in the Amphia Hospital, Breda and the St. Antonius Hospital, Nieuwegein.

Study burden and risks

In each patient seven blood samples will be drawn for analysis. During the

first 24 hours blood samples will be collected using an arterial line which is routinely used in patients undergoing lung surgery. On day two and three blood samples will be drawn simultaneously with standard postoperative sampling. There are no direct risks or benefits for patients included in the study. Clinicians are blinded for the laboratory results determined for the purpose of this study. The test results will therefore not affect treatment of study patients.

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

Elective pulmonary surgery (pneumonectomy, (bi)(sleeve)lobectomy, segmentectomy) for cancer, American Society of Anesthesiologists (ASA) physical status classification >=2 with a planned postoperative admission to the Intensive Care.

Exclusion criteria

(suspected) Infection at the time of surgery and reoperation within 24 hours of surgery

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-11-2018
Enrollment:	250
Type:	Actual

Ethics review

Approved WMO Date:	23-04-2018
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-01-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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
CCMO	NL64754.101.18