Chirurgische behandeling van niet-kleincellig longcarcinoom (NSCLC): thoracoscopisch ondersteunende minithoracotomie (VAMT) versus spiersparende thoracotomie (MST)

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Ethische beoordeling	Goedgekeurd WMO
Status	Werving nog niet gestart
Type aandoening	Ademhalingsorgaan- en mediastinale neoplasmata maligne en niet-gespecificeerd
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON29990

Bron
ToetsingOnline

Verkorte titel
VAMT studie

Aandoening

- Ademhalingsorgaan- en mediastinale neoplasmata maligne en niet-gespecificeerd
- Luchtwegneoplasmata
- Luchtwegen therapeutische verrichtingen

Synoniemen aandoening
longkanker, non-small cell lung cancer

Betreft onderzoek met

Mensen

Ondersteuning

Primaire sponsor: St. Antonius Ziekenhuis
Overige ondersteuning: Ministerie van OC&W

Onderzoeksproduct en/of interventie

Trefwoord: NSCLC, spiersparende thoracotomie, VAMT lobectomie

Uitkomstmaten

Primaire uitkomstmaten

Pain

(1) Visual Analogue Scale: 1-100 mm and/or (2) amount of epidural analgesia

during 48 hours postoperatively: dose/10kg/hour.

We have chosen pain (VAS) as the primary endpoint because we hypothesize that

VAMT results in less pain due to a smaller incision and the use of a soft

tissue retractor in stead of a rib retractor resulting in less traction applied

on the ribs finally decreasing postoperative pain levels and blood loss. We

therefore hypothesize that a faster mobilization is expected resulting in

faster discharge, less morbidity (and possibly mortality), better lung function

tests and lower immunological response. In fact, we believe that most secondary

endpoints are primarily influenced by pain, the primary endpoint. Furthermore,

from endpoints like 5-year survival and duration of chest tube drainage we do

not have a hypothesis which technique is the best.

NB: Pain policy

The currently applied (in this hospital) pain protocol for thoracotomy will be

implemented in this study (advisory: dr. P Bruins, anaesthesiologist).

1. All patients receive epidural analgesia (bupivacain 0.125% and sufentanyl 1 µg/mL) during 48 hours postoperatively. The analgesia will be infused at 6-8 mL/hour (bupivacain: 1mg/10kg/hour and sufentanyl: 0.8 µg/10kg/hour).
After 48 hours, the epidural catheter will be removed and all patients will receive paracetamol 4dd1g until discharge. If additional morfine is necessary, it must be noted on the **invulformulieren**.

2. If epidural analgesia can not be applied (insertion technically impossible, anticoagulation, epidural failure, patient refusal or any other reason), intravenous infusion of morfine will be administered by patient-controlled analgesia (PCA) during 48 hours postoperatively.
After 48 hours, all patients will receive paracetamol 4dd1g until discharge. If additional morfine is necessary, it must be noted on the **invulformulieren**

Secundaire uitkomstmaten

· 5-year survival (Kaplan Meier analysis)

· Quality of life (SF-36)

· Incision length (centimeters)

· Operation time (incision-closure: minutes)

· Blood loss (per and postoperatively: mL) and transfusion (units)

· Chest tube drainage duration (days)

· Leucocyte count, CRP

· Complications (pneumonia, atelectasis, sepsis, death, wound infection, wound herniation: number of complications per group)

· Discharge (days)

· Restart ADL and professional activities (days)

· Recurrences (period between intial operation and diagnosis of recurrence:

months)

· lung function tests (FEV1, VC)

Toelichting onderzoek

Achtergrond van het onderzoek

Cancer is the leading cause of death before the age of 85 years resulting in more than half a million deaths per year in the United States [1]. In 2005, primary lung cancer was the second leading cancer type in the United States with approximately 190,000 new cases to be estimated for 2006. Among all cancer types, lung cancer has the highest death rate [1].
Lung cancer is usually treated by surgical resection and/or cytostatic drug administration depending on the disease stage. Stage I (a and b) and II non-small cell lung cancer (NSCLC) are currently treated by surgical resection and adjuvant cytostatic therapy resulting in a 5-year survival of 75, 60 and 40% respectively [2].
Anatomical lobectomy with mediastinal lymph node staging is the generally accepted treatment for patients with stage I and II NSCLC [3]. Sublobar resections like segmentectomy or wedge resection result in a higher local recurrence rate probably due to micrometastatic lymphogenic disease present at the moment of surgery [3]. In contrast, the type of resection for pulmonary metastases does not affect survival [4].
Since 1992, an increasing number of papers report of video-assisted lobectomy (VATS) in stead of conventional thoracotomy for the treatment of stage 1 NSCLC. VATS is defined as *complete* if surgery is performed completely by visualization through a television monitor. However, certain types of operations like segmentectomy and bronchoplasty (sleeve resection) are very difficult to perform using the *complete** technique. In contrast, **hybrid VATS or video-assisted mini-thoracotomy (VAMT)* is a compromise between VATS and conventional thoracotomy and combines surgical view by television monitoring and direct vision using a muscle-sparing mini-thoracotomy [5]. Currently, less than 5% of all lobectomies are performed using the VATS technique [6].
Short-term advantages of VAMT using a rib retractor are shown in most retrospective studies such as decreased pain and blood loss, shorter chest tube drainage, less immunological respons, lower complication rate, lower hospital charges, shorter hospital admission and better pulmonary function tests postoperatively [7,8,9,15]. Other studies, including two prospective trials

(one of them was not randomized) failed to show advantages of lobectomy by VAMT compared to muscle-sparing thoracotomy (MST) [11,16,17].
On the other hand, operation time is often longer compared to conventional thoracotomy [8] and conversion sometimes occur due to mediastinal lymph node involvement, adhesion, bleeding or anomaly that are all also depending on the experience of the surgeon [10]. But we hypothesize that in case of more experience, the operation time could even be shorter than with a conventional thoracotomy. Furthermore, the adequacy for complete lymph node dissection by VAMT is controversial [11,12]. Yamashita showed a higher chance of seeding tumour cells into the circulation during VAMT compared to open surgery [13]. However, very little is known about the adequacy on long-term survival of VAMT. Some retrospective studies describe promising 5-year survival rates between 64-97% for stage I disease that should be interpreted carefully because of the risk of understaging due to very strict selection criteria [14,15]. The occurrence of entmetastases, known as a possible complication of oncological VAMT surgery, has never been described.

At present, prospective randomized trials failed to show advantages of lobectomy by VAMT using a rib retractor compared to MST. Therefore, this study evaluates short- and long-term outcome of patients suffering from stage I and IIa NSCLC prospectively randomized for lobectomy by VAMT without the use of a rib retractor or by MST.

NB: We hereby declare that this study will performed according the approved protocol by the ethics committee (VCMO, Sint Antonius Ziekenuis Nieuwegein), ICH-GCP and the WMO regulations.

Doel van het onderzoek

At present, retrospective studies suggest short-term advantages of lobectomy by video-assisted minithoracotomy compared to muscle-sparing thoracotomy for the treatment of non-small-cell lung cancer like less blood loss and less pain postoperatively. However, one randomized prospective trial failed to show advantages of VAMT lobectomy using a rib retractor while another prospective non-randomized trial using a rib retractor showed short-term advantages. We hypothesize that lobectomy by VAMT without rib retractor results in less pain (page 4-6 protocol). Therefore, we propose a prospective randomized trial evaluating short- and long-term outcome of patients suffering from stage 1 and 2a non-small cell lung cancer treated by lobectomy by VAMT without rib retractor or by MST.

Onderzoeksopzet

Design: prospective, randomized, open
Duration: for each patient 5 years
Expected inclusion period: 2 years (total study duration: 7 years): the

inclusion period is expected to start from 01-01-2007 tot 01-01-2009; the study will finish 5 years later (01-01-2014)
Flow chart (see addendum):
a. Day 0
· quality of life: SF-36 (nulmeting)
· operation (lobectomy by VAMT or MST)
· at 8 hours postoperatively: VAS or mL used
b. Day 1 and 2
· 2 times/day: VAS or mL used
c. Day 3-discharge
· 3 times/day VAS
d. Days 0, 1, 2, 5 and 8
· lab: CRP and leucocytes
e. Day 7: quality of life: SF-36
f. 1 month after discharge
· consultation pulmonologist
· quality of life: SF-36
· physical examination
g. 3 months after discharge
· physical examination
· quality of life: SF-36
· pulmonary function tests
d. 3 and 5 years after discharge
· physical examination
· quality of life: SF-36

Onderzoeksproduct en/of interventie

VAMT or MST

Inschatting van belasting en risico

waarschijnlijk leidt de te testen techniek (VAMT) tot minder pijn, complicaties en kortere opnameduur tov de standaard behandeling

Contactpersonen

Publiek

St. Antonius Ziekenhuis

Koekoekslaan 1
Nieuwegein

NL

Wetenschappelijk

St. Antonius Ziekenhuis

Koekoekslaan 1
Nieuwegein
NL

Locaties

Landen waar het onderzoek wordt uitgevoerd

Netherlands

Deelname eisen

Leeftijd
Volwassenen (18-64 jaar)
65 jaar en ouder

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

Stadium 1a, 1b and 2a NSCLC (T1: <= 3cm)
De operatie-indicatie wordt gemaakt op basis van de diagnose en comorbiditeit; vervolgens kan de patient na het verkrijgen van toestemming van de patient (informed consent) worden geincludeerd in de studie. Dus als de patient in staat is om geopereerd te worden, kan hij/zij geincludeerd worden op basis van de in-/exclusiecriteria die op deze bladzijde geformuleerd zijn.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

Stadium 2b NSCLC en hoger, Centrale locatie van de tumor, Sleeve resectie noddzakelijk, Segment resectie, leeftijd boven 18 jaar (echter, NSCLC is nooit beschreven op de kinderleeftijd), patienten die mentaal niet in staat zijn om aan te geven of ze met de studie mee willen doen.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel
Doel:	Behandeling / therapie

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	15-08-2006
Aantal proefpersonen:	50
Type:	Verwachte startdatum

Ethische beoordeling

Goedgekeurd WMO

Soort:	Eerste indiening
Toetsingscommissie:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
CCMO	NL13068.100.06