Study protocol

Endosonography versus Mediastinoscopy for Mediastinal Nodal Staging of Lung Cancer: Survival in the ASTER Randomized Clinical Trial

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Introduction
Mediastinal nodal staging is key in the management of patients with non-small cell lung cancer (NSCLC) as it directs therapy and has prognostic value. For many years, mediastinoscopy was considered the ‘gold standard’ in the mediastinal staging of patients with NSCLC. Recently international guidelines have been changed and the first step in the mediastinal nodal staging process now consists of endoscopic techniques (endobronchial ultrasound (EBUS) and transesophageal ultrasound (EUS)) for patients with suspected lymph nodes on CT-PET imaging.\(^1,2\) In the absence of mediastinal metastases at EBUS and/or EUS, confirmatory mediastinoscopy is recommended.\(^3\)

The results of the ASTER trial (Assessment of Surgical Staging vs Endosonographic Ultrasound in Lung Cancer: a Randomized Clinical Trial) have been a major driver in the implementation of endosonographic techniques in the mediastinal staging strategy of patients with NSCLC. This trial compared a surgical staging strategy (mediastinoscopy) with an endosonographic staging strategy (combined use of EBUS and EUS, if negative followed by mediastinoscopy), and demonstrated that mediastinal staging was significantly more accurate for patients randomized to the endosonographic staging strategy (sensitivity 94% versus 79%).\(^4\) A subsequent cost-effectiveness study showed that the endosonographic staging strategy also resulted in higher quality-adjusted life years over 6 months and at lower costs.\(^5\)

To date, it is unknown whether improved staging results in a survival benefit. As far as we know, there are no studies that have examined whether the long-term survival (>5 years) is actually better in the group of patients who underwent the more accurate endosonographic staging strategy compared to the surgical staging strategy.

Objective
To analyze survival data in the ASTER trial.

Hypothesis
An endosonographic staging strategy results in improved 5 year lung cancer survival compared to a surgical staging strategy.
Methods
The ASTER trial was registered at ClinicalTrials.gov (identifier NCT00432640). The current analysis is a post-hoc analysis of the ASTER trial. The outcomes described in this post-hoc analysis were not pre-defined in the original protocol.4

Data collection
Data collection will be performed in 2015, which is more than 5 years after the date of randomization of each patient in the ASTER trial, which recruited patients from February 2007 to April 2009.

For the current analysis, we aim to obtain the following data for each patient included in the ASTER trial:

- Alive (yes/no)
- In case of death: the date and cause of death
- In case the current alive status cannot be determined: the date the patient was last known to be alive (where we will aim to obtain survival data at least 5 years after randomization)

These data will be obtained by searching the patient records in the participating hospitals in Leuven, Gent, Leiden and Cambridge. If data cannot be found in these records, death registries will be searched or known specialists or general practitioners will be contacted.

Data will be collected using a worksheet that was developed for this post-hoc analysis of ASTER (Appendix 1).

Ethical approval
Waiver of ethics review is applicable for this post-hoc analysis as at least 5 year follow-up of patients with lung cancer is advised in The Netherlands, Belgium and the UK. At inclusion in the ASTER trial, all participants provided written informed consent.
Main outcome

Five year survival for the endosonographic versus the surgical staging strategy.

Statistics

We will calculate the proportion of survivors five years after randomization for both staging strategies, and calculate odds ratios with 95% confidence intervals. Patients with missing survival data at 5 years will be excluded from this analysis.

We will also perform Kaplan-Meier analysis to compare median survival between the two staging strategies. In this analysis, patients for whom we did not obtain a date of death will be censored on the date they were last known to be alive. This means that if we record that a patient was last known to be alive within the first five years after randomization, the patient will be included in this analysis.

We will perform subgroup analysis for patients with nodal stages N2/N3 and N0/N1.

Data will be analyzed using SPSS version 22 (SPSS Inc, Chicago, Illinois).
References


