Endosonography-related mortality and morbidity for pulmonary indications: a nationwide survey in the Netherlands

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Background: Endosonography is being implemented rapidly in pulmonary medicine for the diagnosis and staging of lung cancer, the assessment of sarcoidosis, and the assessment of mediastinal lesions. Although serious adverse events (SAEs) have been described, safety data outside cohort studies are scarce.

Objective: To assess the SAE and mortality rate of EUS-guided FNA (EUS-FNA) and endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA) for mediastinal and/or hilar analysis.

Design: Nationwide, retrospective survey by using questionnaires.

Setting: All hospitals in the Netherlands.

Patients: All patients undergoing EUS-FNA and EBUS-TBNA for intrathoracic analysis in the period 1999 to 2011.

Interventions: EUS-FNA and EBUS-TBNA.

Main Outcome Measurements: Occurrence of fatal outcomes and SAEs. Detailed information was obtained for each reported case, and all cases were reviewed independently by 2 investigators, including identification of risk factors.

Results: All 89 hospitals (100%) responded. An estimated 14,075 EUS-FNA and 2675 EBUS procedures were performed. Seven patients died after endosonography (5 EUS-FNA, 2 EBUS [mortality rate 0.04%]). All fatalities occurred in patients of poor performance status (American Society of Anesthesiologists Physical Status Classification System score of III/IV). Twenty-five SAEs were reported (22 EUS-FNA, 3 EBUS [SAE rate of 0.15%; EUS-FNA 0.16%, EBUS 0.11%]). SAEs were mostly (64%) of infectious origin. No specific risk factors for infectious adverse events could be identified.

Limitations: Retrospective study, possible recall bias, overrepresentation of EUS-FNA cases.

Conclusion: Endosonography appears to be a safe technique for the analysis of mediastinal and/or hilar lesions. Poor performance status is a risk factor for fatal outcomes. Mediastinitis and/or mediastinal abscess formation is rare but is a potential and dangerous adverse event of endosonography. (Gastrointest Endosc 2015;82:1009-15.)

Endosonography (EUS-guided FNA [EUS-FNA]) and endobronchial US–transbronchial needle aspiration (EBUS-TBNA) is an increasingly used diagnostic technique in patients in whom tissue verification of intrathoracic lymph nodes is indicated for the diagnosis and staging of lung cancer, the assessment of sarcoidosis, or the analysis of mediastinal masses.

Lung cancer staging guidelines recommend endosonography as the initial tissue staging test after CT or positron emission tomography (PET) to detect mediastinal node

Abbreviations: COPD, chronic obstructive pulmonary disease; CTCAE, Common Terminology Criteria for Adverse Events; EBUS, endobronchial US; EUS-FNA, EUS-guided FNA; PET, positron emission tomography; SAE, serious adverse event; TBNA, transbronchial needle aspiration.

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TABLE 1. Severity score of EBUS-related adverse events*

Severity	Grade
Mild: asymptomatic or mild symptoms, clinical or diagnostic observations only, intervention not indicated	1
Moderate: minimal, local, or noninvasive intervention indicated	2
Severe or medically significant but not immediately life-threatening: hospitalization or prolongation of hospitalization indicated	3
Life-threatening consequences: urgent intervention indicated	4
Death related to adverse event	5
EBUS was judged as a contributing factor to the fatal outcome	A
EBUS was judged as the major cause of the fatal outcome	B

In addition to the CTCAE classification, we subdivided death (grade 5) into death accelerated by EBUS (A) and death as a direct result of EBUS (B).
EBUS, Endobronchial US.
*Adapted from the Common Terminology Criteria for Adverse Events (version 4.0).[17]

disease.[1] Subsequent surgical staging is indicated in those patients with suspected node involvement in whom endosonography did not find metastases. For the detection of granulomas in patients with suspected sarcoidosis, endosonography is superior to conventional bronchoscopic techniques.[2,3] The large body of evidence regarding the use of endosonography-guided mediastinal node aspiration[4,5] results in rapid implementation. With over 1.8 million new cases of lung cancer worldwide each year[6] and an estimated prevalence of sarcoidosis ranging from 1 to 40 cases per 100,000 population,[7] it is expected that several hundreds of thousands of mediastinal endosonography procedures will be performed annually. Besides diagnostic test characteristics, safety and adverse events of novel techniques are of major importance. In a recent literature review, few serious adverse events (SAEs) after endosonography were reported.[8] However, SAEs have been described in several case reports,[9-14] including suggestions of endosonography-associated fatalities.[15,16] In the current implementation phase of endosonography, insight into SAEs, including identification of risk factors, is important. However, data on safety outside of clinical trial settings are scarce.

Therefore, we conducted a nationwide, retrospective survey of all mortality and SAEs related to EUS-FNA and EBUS procedures performed in the Netherlands over a 12-year period.

MATERIALS AND METHODS

Data collection

We conducted a nationwide survey by sending questionnaires to all 89 hospitals (both performing and referring EBUS/EUS-FNA centers) in the Netherlands during 2010 to 2011. The questionnaires requested that respondents report SAEs. One questionnaire was designed for those clinics performing EUS-FNA and/or EBUS, the other for those referring patients for the procedures. In case SAEs were reported, additional detailed information including endoscopy and radiologic reports as well as relevant medical correspondence was obtained.

Definitions of outcomes

All fatal outcomes and SAEs were assessed independently by the two physicians and classified according to severity of the adverse events according to Common Terminology Criteria for Adverse Events (CTCAE) (Table 1).[17] All events were discussed, and the treating physician was consulted in case further clarification was indicated.

SAEs were defined as adverse events threatening the health of the patient, either concerning an active problem requiring intervention to avert further damage (eg, severe infection, esophageal laceration) or an unforeseen event causing no harm in this particular case but having serious potential to do so (eg, mediastinal hematoma). SAEs were subdivided into grades 2, 3, 4, or 5 by using the CTCAE grading scale and included death, mediastinitis, bleeding, severe respiratory failure, perforation, empyema, and equipment misuse as well as adverse events that may lead to clinical deterioration such as drug intoxication or aspiration. An invasive intervention was defined as any procedure in which there was a break in the skin or there was contact with the mucosa or any internal body cavity. These included surgery, pleural drainage, gastroscopy, and so forth. A noninvasive or minimally invasive intervention included investigations such as blood oxygen saturation, venous puncture, or radiographic scanning. A hospital admission was defined as at least an overnight stay.

Statistical analysis

SAEs and mortality rates of EUS-FNA and EBUS were calculated by dividing the sum of adverse events by the average of the sum of the lower and upper limits of the reported estimations of performed procedures. The Chi-square and Fisher exact tests were used for the analysis of categorical data. All analyses were performed with SPSS (version 17.0, Chicago, Ill, USA).

RESULTS

Completed questionnaires from all 89 Dutch hospitals were collected. Forty-three of 89 clinics (48%) performed