

## Transaortic EUS-guided FNA in the diagnosis of lung tumors and lymph nodes

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**Background:** Obtaining tissue from a para-aortic lymph node or tumor is a challenge that currently requires invasive surgical procedures. Para-aortic lung tumors can be clearly visualized by EUS. Although the accessibility of lesions adjacent to the esophagus is well documented, the para-aortic region has never been systematically explored.

**Objective:** To assess the feasibility, yield, and safety of transaortic biopsy specimens in the diagnosis of lung tumors and nodal masses located lateral to the aorta.

**Design:** A retrospective case series of 14 consecutive patients.

**Setting:** Pulmonary Department, Leiden University Medical Center, Leiden, The Netherlands.

**Patients:** Fourteen patients with known or suspected lung cancer. Nine patients presented with a left-sided lung mass (mean size 27 mm), whereas 5 patients had an enlarged para-aortic node (mean size 16 mm).

**Interventions:** Real-time EUS-guided transaortic biopsy of a para-aortic lesion.

**Main outcome measurements:** Feasibility, diagnostic yield, and complication rates of transaortic EUS-guided FNA (EUS-FNA).

**Results:** The final diagnosis was known in 12 patients (10 non-small-cell lung carcinoma [NSCLC], 1 small-cell lung carcinoma [SCLC], and 1 renal-cell carcinoma). EUS-FNA established malignancy in 9 of 14 patients (64%) (8 NSCLC and 1 SCLC). One aspirate revealed reactive nodal tissue, and 4 demonstrated nonrepresentative material. Malignancy was further assessed in 3 patients after subsequent diagnostics. Transaortic FNA was found to be safe. In 2 patients, EUS images after biopsy were suspicious for a small para-aortic hematoma. These patients recovered uneventfully.

**Conclusions:** These results demonstrate that a single EUS-guided transaortic biopsy of para-aortic lymph nodes and tumors is a feasible and probably safe method that results in a diagnosis in the majority of cases.

Obtaining a tissue diagnosis from a lung tumor or a mediastinal lymph node located lateral to the aorta traditionally has been regarded as a diagnostic challenge because of the interposition of the aorta. Surgery (mediastinotomy, thoracotomy, or video-assisted thoracic surgery [VATS]) is

*Abbreviations:* EUS-FNA, EUS-guided FNA; NSCLC, non-small-cell lung carcinoma; LUMC, Leiden University Medical Center; PET, positron emission tomography; SCLC, small-cell lung carcinoma; VATS, video-assisted thoracic surgery.

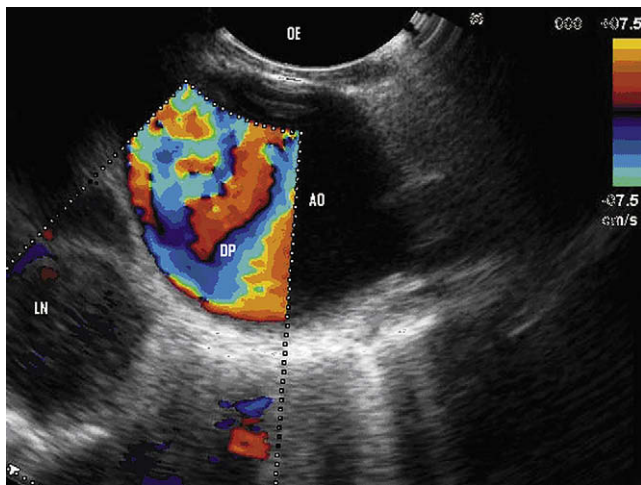
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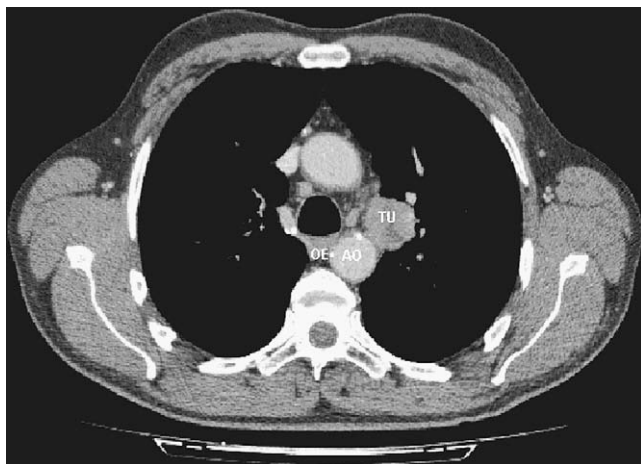
frequently required for the diagnosis of these lesions.<sup>1,2</sup> However, these procedures are invasive and costly and require hospital admittance.

Tumors and mediastinal lymph nodes located in the para-aortic region can easily be identified by esophageal EUS, because the aorta provides an excellent medium to transfer US waves (Fig. 1).

Paraesophageal lymph nodes and centrally located intrapulmonary tumors can accurately be aspirated by using EUS-guided FNA (EUS-FNA).<sup>3,4</sup> To date, it is unknown whether it is feasible and safe to biopsy intrapulmonary lung tumors and mediastinal lymph nodes through the aorta with EUS-FNA. Therefore, we aimed to evaluate the feasibility, yield, and safety of EUS-guided transaortic FNA of lung tumors and para-aortic lymph nodes.



**Figure 1.** EUS image from the esophagus (OE), demonstrating lymph node station 6 (LN) located lateral to the aorta (AO). Doppler flow (DP) is seen in the aorta.

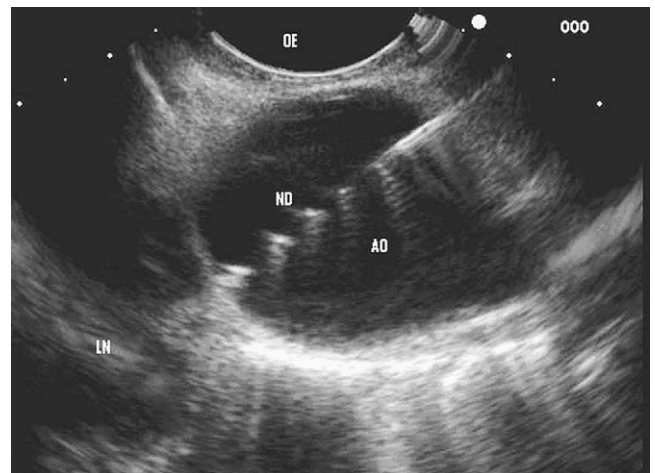


**Figure 2.** CT image, demonstrating a para-aortic lung tumor (TU). OE, esophagus; AO, aorta.

## PATIENTS AND METHODS

Fourteen consecutive patients with suspected ( $n = 13$ ) or proven malignancy ( $n = 1$ ) who underwent transaortic FNA of a mass located adjacent to the aorta were retrospectively included in this case series between April 2003 and April 2008. Informed consent was obtained in all cases, and, in all cases, the para-aortic lesion was the only site suspicious for malignancy (Fig. 2). Based on the available CT and positron emission tomography (PET) imaging, a transesophageal biopsy of the lesion performed through the aorta was regarded as the only option to diagnose or stage these patients by means of a minimally invasive procedure.

In the majority of the cases, the lesion punctured under echo guidance was a suspected primary lung tumor situated lateral to the aorta (4 left lower lobe, 4 left upper



**Figure 3.** Real-time EUS-guided transaortic aspiration of a para-aortic lymph node (LN). The needle (ND) is well visible within the aorta. OE, esophagus; AO, aorta.

lobe, 1 lingula). One patient presented with a para-aortic mass suspicious for a metastasis from a renal-cell carcinoma. The remaining 5 patients underwent transaortic FNA for an enlarged para-aortic mediastinal lymph node (mean size on CT 16 mm, range 10-20 mm), suspicious for N2 disease (node 6,  $n = 3$ ; node 5,  $n = 2$ ).

EUS-FNA procedures were performed at the Department of Pulmonary Medicine of the Leiden University Medical Center (LUMC) by 2 experienced investigators (J.T.A., K.F.R.) on an outpatient basis with the patient under moderate sedation with midazolam (0-5 mg intravenously). The LUMC is a tertiary-care hospital, and the pulmonary department is a referral center for the analysis of mediastinal lesions by EUS-FNA. Investigations were performed by using a Pentax FG 34 UX echoendoscope (Pentax, Breda, The Netherlands), with a longitudinal convex US transducer that had an adjustable US frequency of 5, 7.5, or 10 MHz, in combination with a Hitachi EUB 6500 US scanner (Hitachi Ultrasound, Reeuwijk, The Netherlands). All aspirates were obtained under real-time US-guided FNA by using a 22-gauge needle (type Hancke/Vilmann; GIP/MEDI-Globe, Achenmühle, Germany).

During the EUS procedure, the investigators first systematically assessed all mediastinal nodal stations detectable from the esophagus. When no suspicious lesion was seen other than the mass in the para-aortic region, Doppler flow was applied to distinguish the lung mass or node from the aorta (Fig. 1). Before any transaortic FNA, we first tried to mobilize the esophagus, by deflecting the tip of the endoscope, to try to position the EUS endoscope immediately adjacent to the target lesion. In case the transaortic route was the only option, a single real-time biopsy of the lung mass or lymph node was performed in the absence of intraluminal aortic plaques. Vacuum suction was applied as soon as the tip of the needle reached the target lesion. After retracting the

**TABLE 1. Patient characteristics, EUS-FNA findings, and follow-up**

Case no.	Sex/age (y)	Mass	EUS cytology of mass	Short axis of mass (mm)	Final diagnosis of the mass
1	F/52	LLL	NSCLC	20	NSCLC*
2	M/77	Node 6	Reactive nodal tissue	10	NSCLC†
3	F/49	LUL	Adenocarcinoma	20	Adenocarcinoma†
4	M/72	Node 6	Erythrocytes	20	Information not available
5	F/66	Node 5	NSCLC	15	NSCLC*
6	M/75	LUL	NSCLC	46	NSCLC*
7	M/71	LLL	NSCLC	40	Squamous carcinoma†
8	F/51	LLL	Lytic material	26	Adenocarcinoma†
9	F/65	LUL	SCLC	13	SCLC*
10	F/52	Node 6	Squamous epithelial cells	14	Information not available
11	F/63	LLL	NSCLC	35	Adenocarcinoma†
12	F/49	LUL	Erythrocytes	15	Renal-cell carcinoma†
13	F/51	Lingula	NSCLC	25	NSCLC*
14	M/57	Node 5	NSCLC	20	NSCLC*

LLL, Left lower lobe; LUL, left upper lobe.

\*Based on cytology EUS, no further surgical confirmation.

†Confirmative surgical pathology of mass biopsied on EUS.

needle, the para-aortic area was observed on echo images for 3 minutes to assess for immediate procedure-related complications, and the aspirate was put on both glass slides, as well as in a fixative for cell block evaluation. One of the endoscopists evaluated the representativity of the aspirates during the procedure by using on-site cytology.

The applied criterion standard for the involvement of malignancy in the target lesion was determined either by the presence of malignant cells in the cytologic material obtained by EUS-guided transaortic FNA or by subsequent surgical-pathologic confirmation of the para-aortic lesion. False-positive EUS aspirates were considered highly unlikely.

**OBSERVATIONS**

In all 14 patients, real-time visualization of the needle through the aorta into the target lesion was achieved (Fig. 3), and aspirates were obtained in all subjects. Patient characteristics, EUS-FNA findings, and follow-up are presented in Table 1. A single transaortic FNA was confirmative for malignancy in 9 patients (64%). Seven of those patients had a suspected primary lung tumor, and aspirates of those tumors revealed large-cell undifferentiated carcinoma (n = 5), adenocarcinoma (n = 1), and small-cell lung carcinoma (n = 1). The other 2 patients in whom EUS-FNA found malignancy had a mediastinal para-aortic lymph node and aspirates that showed large-cell undifferentiated

carcinoma in both cases. For the 5 patients in whom transaortic EUS-FNA did not find malignancy in the para-aortic lesion, biopsy specimens disclosed erythrocytes (n = 2), reactive nodal tissue (n = 1), squamous epithelial cells from the esophagus (n = 1), and lytic material (n = 1). These 5 patients underwent subsequent surgical staging (3 thoracotomies, 1 mediastinotomy, and 1 VATS), and malignancy was found in 3 of the 5 patients.

In the 2 remaining cases, metastatic disease was found in a site other than the para-aortic area, and, therefore, no final tissue diagnosis was obtained from this lesion.

In 2 patients (Table 1, case nos. 10 and 14) a para-aortic extravasate compatible with a local hematoma was observed on echo images immediately after transaortic FNA. One patient complained of chest discomfort for a short duration, whereas the other subject remained asymptomatic. The former patient was admitted overnight, and a CT was performed the next day to exclude aortic dissection. The CT images demonstrated a para-aortic hematoma (maximal short-axis diameter of 2 cm), without evidence of aortic dissection.

**DISCUSSION**

This case series demonstrates the feasibility of transaortic aspiration in para-aortic lesions under real-time controlled EUS guidance. A single EUS-guided transaortic FNA

was diagnostic for malignancy in 64% of the patients. The yield in the current study is somewhat lower than other studies that assessed mediastinal node enlargement and centrally located intrapulmonary masses by EUS-FNA.<sup>3-5</sup> This, however may be explained by the fact that only a single attempt at transaortic FNA was made in all patients. For mediastinal nodal staging, a prospective study showed that, for an optimal diagnostic yield, at least 5 biopsies should be performed.<sup>6</sup> On-site cytologic evaluation of the aspirate may probably increase the diagnostic yield of transaortic FNA.

Lymph nodes and tumors at the contralateral side of the aorta can be easily visualized through the blood interface of the vessel. However, small lymph nodes in this region (Fig. 3) are located quite some distance from the echo probe, which makes it sometimes difficult to find the right angle when inserting the biopsy needle.

To our knowledge, this is the first study of EUS-guided transaortic FNA for the diagnosis and staging of lung cancer. Wallace et al<sup>7</sup> recently published a case report of 1 transaortic FNA, which obtained a diagnosis of lung carcinoma without complications. Nevertheless, the procedure of puncturing through the aorta is not a novel method. Ischia et al<sup>8</sup> reported a transaortic celiac plexus block in 28 patients in 1983. In addition, translumbar aortography, a direct percutaneous lumbar puncture of the aorta for diagnostic arteriography of the abdominal aorta, was a common procedure in the 1960s and 1970s. Postprocedure EUS images performed immediately after the puncture demonstrated a para-aortic hematoma in 2 patients.

In the radiology literature, it is not uncommon that small retroperitoneal hematomas develop after translumbar aortography. However, clinically important bleeding only occurred in 0.1% to 0.5% of the cases when 20-gauge needles were used.<sup>9</sup>

In a review article of 14,550 patients who underwent translumbar aortography, the investigators documented 7 major (0.05%) and 2 fatal (0.014%) complications.<sup>10</sup> Although this article suggests that the development of hematomas is not uncommon and, in general, the bleeding does not require clinical intervention, it still warrants caution for future EUS-guided transaortic biopsies, because the precise morbidity rates remain uncertain. Whether 25-gauge needles will reduce the bleeding risk and, meanwhile, provide a similar diagnostic yield, is unknown.

If transaortic FNA is considered, then extra caution should be taken when echo images show aortic calcifications suggestive of aortic atherosclerotic plaques. In this scenario, transaortic FNA could lead to the dislocation of the plaque, which results in embolism of small arteries. The latter may cause a "blue toe syndrome"<sup>11</sup> but may also result in more severe complications, such as subacute renal failure and intestinal ischemia.<sup>12</sup> In addition, it is unknown whether hematogenous tumor seeding can occur if a lesion is biopsied through a vessel. Therefore, the

number of needle passes should be reduced to the minimum.

Another hypothetical risk is the laceration of the aortic wall that results in aortic dissection. Para-aortic lung tumors and lymph nodes can also be diagnosed by parasternal mediastinotomies or by a left-sided VATS. Mediastinotomy, also known as the Chamberlain method, is considered to be a valuable technique nowadays for the evaluation of lesions in the aortopulmonary window. Best et al<sup>13</sup> performed a study that evaluated the yield and safety of 62 anterior mediastinotomies and found a sensitivity of 98% and specificity of 64.5%. The morbidity rate in this study was 16.1% (wound infection 6.5%, life threatening hemorrhage 3.2%, left vocal cord paralysis 3.2%, and atelectasis left lower lobe 1.6%), and the mortality rate was 1.6%.<sup>13</sup>

Another method to assess the para-aortic region for malignant disease is left-sided VATS. In a large complication study of 895 patients who underwent video-thoracoscopy for several indications (569 cases were lung operations), complication rates were as high as 14% (dysrhythmia 6.1%, prolonged air leak 4.7%, respiratory failure, and/or pneumonia 1.8%).<sup>14</sup> Cerfolio et al<sup>1</sup> performed a retrospective study on 39 patients with VATS for the analysis of N2 disease in the aortopulmonary window and demonstrated a sensitivity of 100%. Transaortic FNA should only be performed in the absence of alternative minimally invasive diagnostic procedures. The technique of obtaining a tissue diagnosis from a para-aortic lesion requires skill and expertise in performing EUS-FNA, and whether less-experienced investigators can perform a diagnostic transaortic FNA of a mass in the para-aortic area remains uncertain.

In conclusion, these results show that transaortic FNA is a feasible and probably safe method for obtaining a tissue diagnosis from a lung tumor or a mediastinal lymph node. However, these results should be interpreted clinically and with caution, and it is of utmost importance that, to agree on the indication when transaortic biopsy is considered, EUS-FNA investigators should find a balance between safety and diagnostic benefit, as well as between the risks and morbidity of surgical-staging procedures.

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