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Scientific letter

Assessment of Feasibility and Prognostic Value of Sentinel Lymph Node Identification by Near-Infrared Fluorescence in Non-Small Cell Lung Cancer in Patients Undergoing Robotic Anatomic Lung Resections

Evaluación de la factibilidad y el valor pronóstico de la identificación del ganglio centinela mediante fluorescencia cercana al infrarrojo en pacientes sometidos a resecciones pulmonares anatómicas robóticas por cáncer de pulmón no microcítico

Dear Editor,

Radical surgical resection remains the standard for diagnosis, staging, and treatment in patients with localized non-small cell lung cancer (NSCLC).[1] In addition to parenchymal resection, systematic nodal dissection (SND) is recommended.[2] However, SMD is performed in less than 40% of patients with stage I NSCLC[3] and can eventually associate complications such as chylothorax, pleural effusion, bleeding, bronchial fistula, oesophageal injury, and nerve damage.[4]

On the other hand, inadequate staging may result in patients presenting with undiagnosed metastatic nodal disease being classified as having early-stage disease and receiving no further adjuvant treatment, contributing to a 50–60% reduction in 5-year survival and an increase in the incidence of recurrences of 40%.[5,6] Understaging can be attributed to inadequate lymph node sampling, the presence of occult micrometastases and/or inadequate histological processing.[6]

Sentinel lymph node (SLN) biopsy provides the benefit of evaluating lymph nodes with a higher risk of metastatic spread, guiding, and focusing histological analysis towards these high-risk nodes, enhancing the ability to detect micrometastases, and reducing morbidity associated with a non-directed and extensive lymphadenectomy.

Recently, several studies have demonstrated the usefulness of indocyanine green (ICG) and near-infrared (NIR) fluorescence imaging in lymph node mapping in cancer patients.[7,8]

The main objective of this prospective study was to assess the feasibility and prognostic value of SLN mapping by fluorescence imaging with ICG in lung cancer surgery.

A prospective, observational, single-centre study was conducted. The project was approved by our institutional Clinical Research Ethics Committee and all patients signed the written informed consent. The inclusion criteria consisted of adult patients with proven or suspected peripheral surgically resectable NSCLC, without evidence of lymph node disease in the preoperative study who underwent robotic anatomical lung resection with SND between September 2020 and June 2022.

Patients with history of previous contralateral or ipsilateral lung resection were excluded.

The technique consisted of transpleural injection of 1 mL of ICG diluted in 20% human albumin (concentration of 2.5 mg/mL) into the peritumoral area as previously described.[9]

All procedures were performed using the Da Vinci X system (Intuitive Surgical, USA) by two board certified thoracic surgeons. Operative technique was standardized as previously described.[10]

SND was performed in all cases. The FireFly® system was turned on to assess all lymph nodes identified in the operating field. If a lymph node was fluorescent, it was resected, observed ex vivo to confirm its avidity with ICG and sent to the pathology department apart from the other lymph nodes.

The primary endpoint was the identification rate of one or more sentinel lymph node(s) by NIR fluorescence imaging after transpleural injection of ICG. The secondary endpoints were the nodal upstaging rate (cN0 → pN1–N2) and the pathological status of the rest of the lymph nodes in cases of negative SLNs.

A mid-term analysis of the overall survival (OS) and disease-free survival (DFS) was also performed to evaluate the prognostic value of SNL identification.

A total of 24 patients were included (Table 1). No adverse events were detected in relation to the peritumoral injection of ICG.

A SLN was identified in 17 patients (70.8%). The 7 SLN identification failures were attributed to technical issues related to intrapleural spread of the ICG during transpleural injection.

In all cases the SLN was single. In 5 cases, the SLN was located in a N1 interlobar station, in 5 was it was found in a N1 hilar station and in 7 patients it was identified in an N2 mediastinal station.

Further analyses focus on patients who had a successfully identified SNL (17 cases) and whose pathological examination confirmed a primary lung malignancy (14 cases). In one case, invasion of the SLN by metastasis was identified, corresponding to a lymph node upstaging of 7.1%. Two cases with negative SLN had a pN+ result in the definitive histological analysis (one intraparenchymal pN1 case and one skip-N2 metastasis pN2 case (negative SLN in region 11R and N2+ in region 7)).

Only patients with anatomopathological diagnosis of primary lung carcinoma pN0 in the definitive pathological analyses were included ($n = 16$).

The median follow-up was 21.86 months (IQR = 16.90–23.76). OS of the complete series was 100%. DFS was 100% ($n = 11/11$) in the case of pN0 SLNs ($n = 11$), while in cases in which the SLN was not identified ($n = 5$) it was 80% ($n = 4/5$). Recurrence occurred in a patient with stage IA2 adenocarcinoma, and was localized in the liver.

In the current study we reported a SLN identification rate of 70.8% with NIR fluorescence imaging after transpleural injection of ICG. These results are in line with those described by Phillips et al.[11]

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Table 1
Characteristics of the population.

Variable	Population ($n = 24$)
Age (year), median (IQR)	67.9 (75.3–59.5)
Male sex, n (%)	7 (29.2)
Smoking status, n (%)	
Never	4 (16.7)
Former	12 (50)
Current	8 (33.3)
BMI (kg/m^2), median (IQR)	26.26 (28.42–23.52)
FEV1%, median (IQR)	99 (114.5–84.25)
DLCO%, median (IQR)	83 (103–75)
Comorbidities, n (%)	
Cardiopathy	3 (12.5)
Hypertension	8 (33.3)
COPD	4 (16.7)
Diabetes	2 (8.3)
Kidney insufficiency	2 (8.3)
Previous malignancy	10 (41.7)
Cancer clinical stage, n (%)	
IA1 (cT1aN0)	0 (0)
IA2 (cT1bN0)	6 (25)
IA3 (cT1cN0)	9 (37.5)
IB (cT2aN0)	3 (12.5)
IIA (cT2bN0)	3 (12.5)
IIB (cT3N0)	3 (12.5)
Induction treatment, n (%)	1 (4.17)
Surgical resection, n (%)	
Lobectomy	22 (91.7)
Bilobectomy	1 (4.2)
Pneumonectomy	1 (4.2)
Final histopathology, *n* (%)	
NSCLC	21 (87.5)
Adenocarcinoma	16
Squamous cell carcinoma	2
Carcinoid tumour	1
Other subtypes	2
Pulmonary metastases	2 (8.3)
Bening lesion	1 (1)

IQR: interquartile range; BMI: body mass index; FEV1, forced expiratory volume in one second; DLCO: diffusing capacity of the lung for carbon monoxide; COPD: chronic obstructive pulmonary disease; NSCLC: non-small cell lung cancer.

(67.5% of total cases and 77.4% in solid nodules) who also identified some critical factors in the success of SLN detection (injection of at least 1 mg of ICG, combination with albumin, and pulmonary ventilation after injection) and with those published by Stasiak et al.[12] (75%) who found a better identification rate with transbronchial injection of ICG compared with transpleural injection (77.6% vs 68.2%).

Our study shown an upstaging rate of 7.1%. However, two cases with a negative pN0 SLN had nodal metastasis on complementary dissection (one intraparenchymal N1 and one skip-N2 metastasis). Previous similar studies[11–13] reported all patients with a negative pN0 SLN were cancer free on the final pathological analysis indicating that N0 status, when stablished with SLN mapping, reflects the true N0 status. Subsequently, these authors described a better DFS in patients with histologically negative SLN identified, which was also found in our study.

Our study has some limitations that must be taken into account: the small number of patients, the single institution experience, the restriction of surgical approach to robotic, and the short follow-up.

SLN mapping by NIR fluorescence imaging is a safe and feasible technique. This technique may help improve pathological staging and subsequently improve long-term outcomes of surgical NSCLC patients.

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Authors' contributions

Declaration of substantial contributions to:

1. Study conception and design: MTGH, MFJ.
2. Acquisition of data: MTGH, CF, MF, CR, MFJ.
3. Analysis and interpretation of data: MTGH, MFJ.
4. Drafting of the manuscript or critical revision for relevant intellectual content: MTGH, MFJ.
5. Final approval of the version to be submitted: MTGH, CF, MF, CR, MFJ.

Conflicts of interest

The authors declare that there is no conflict of interest regarding the content of this manuscript.

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