



CIRUGÍA ESPAÑOLA

www.elsevier.es/cirugia


Review article

Gastrointestinal Metastasis From Primary Lung Cancer. Case Series and Systematic Literature Review[☆]



Andrea Balla,^{a,b,*} José D. Subiela,^a Jesús Bollo,^a Carmen Martínez,^a Carlos Rodríguez Luppi,^a Pilar Hernández,^a Yuliana Pascual-González,^c Silvia Quaresima,^b Eduard M. Targarona^a

^a Unidad de Cirugía General y Digestiva, Hospital de la Santa Creu y Sant Pau, Universidad Autónoma de Barcelona, Barcelona, Spain

^b Department of General Surgery and Surgical Specialties Paride Stefanini, Sapienza, University of Rome, Roma, Italy

^c Servicio de Neumología, Hospital Universitario de Bellvitge, Universidad de Barcelona, Barcelona, Spain

ARTICLE INFO

Article history:

Received 31 March 2017

Accepted 6 December 2017

Keywords:

Lung cancer

Gastrointestinal metastasis

Surgical management

Systematic literature review

A B S T R A C T

Aim of the present study is to report clinical characteristics and outcomes of patients treated in authors' hospital for GI metastasis from primary lung cancer, and to report and analyze the same data concerning patients retrieved from a systematic literature review.

We performed a retrospective analysis of prospectively collected data, and a systematic review using the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) guidelines.

Ninety-one patients were included, 5 patients from the authors' hospital and 86 through PubMed database using the keywords "intestinal metastasis" AND "lung cancer". The median time between primary lung cancer diagnosis and GI metastasis diagnosis was 2 months and the median overall survival was 4 months.

This group of patients present a poor prognosis and the gold standard treatment is not defined. None of the reported treatments had a significant impact on survival.

© 2018 AEC. Published by Elsevier España, S.L.U. All rights reserved.

[☆] Please cite this article as: Balla A, Subiela JD, Bollo J, Martínez C, Rodríguez Luppi C, Hernández P, et al. Metástasis gastrointestinales de carcinoma pulmonar primario. Serie de casos y revisión sistemática de la literatura. Cir Esp. 2018;96:184–197.

* Corresponding author.

E-mail address: andrea.balla@gmail.com (A. Balla).

Metástasis gastrointestinales de carcinoma pulmonar primario. Serie de casos y revisión sistemática de la literatura

R E S U M E N

Palabras clave:

Cáncer pulmonar
Metástasis gastrointestinales
Manejo quirúrgico
Revisión sistemática de la literatura

El objetivo del presente estudio es describir las características clínicas y el manejo de los pacientes tratados en nuestra institución por metástasis GI de cáncer pulmonar primario; así como realizar una revisión sistemática de casos reportados en la literatura.

Se realizó un análisis retrospectivo de una base de datos prospectiva y revisión sistemática de la literatura utilizando las normas MOOSE (Meta-analysis Of Observational Studies in Epidemiology).

Se incluyeron 91 pacientes, 5 de la base de datos de nuestra institución y 86 de la base de datos PubMed usando las palabras claves «intestinal metastasis» y «lung cancer». La mediana de tiempo entre el diagnóstico de cáncer pulmonar y el diagnóstico de metástasis GI fue 2 meses, la mediana de supervivencia global fue 4 meses.

Este grupo de pacientes presentan mal pronóstico. El tratamiento estándar no se encuentra bien establecido. Ninguno de los tratamientos descritos ha mostrado tener impacto significativo sobre la supervivencia.

© 2018 AEC. Publicado por Elsevier España, S.L.U. Todos los derechos reservados.

Introduction

The lung cancer is the neoplasia with the highest known cancer-related death rate ranging from 18% to 23%.^{1,2} Despite advances in prevention, it has been reported that approximately 50% of cases present metastasis at the time of diagnosis.³ However, due to new technologies in diagnosis and treatment, patients' survival is increased in the recent years, making it easier to develop metastasis in the long-term period.⁴

Several studies in literature, report that gastrointestinal (GI) metastasis from primary lung cancer are uncommon, with an incidence that ranges from 0.3% to 1.7%.⁵ On the other hand, post-mortem studies have estimated that the incidence of this type of metastatic lesions ranges from 4.6% to 14%.^{5,6} This discrepancy, between the estimated incidence in clinical case studies and autopsies, seems to indicate that, in most cases, there are asymptomatic undiagnosed metastasis.³

Despite the increasing of clinical publications in the literature, there is no still consensus regarding the management of these patients due to their high associated mortality.⁷ It has been estimated that GI metastasis represent a prognostic sign that occurs late in the lung cancer course.³ In addition, due to the difficulty in its clinical detection, it is complex to develop prospective studies and, due to the poor reported literature, principally case report and retrospective studies,⁸ until today an adequate diagnostic and therapeutic data to improve patients' prognosis are missing.

The aim of the present study is to report clinical characteristics and outcomes of patients treated in authors' hospital for GI metastasis from primary lung cancer, and to report and analyze the same data concerning patients retrieved from a systematic literature review.

Methods

This study is a retrospective analysis of prospectively collected data of patients with GI metastasis from lung primary cancer treated in the authors' center (Hospital de la Sant Creu i Sant Pau, Barcelona, Spain) between 2012 and 2017. All patients admitted to authors' center sign an informed consent where they authorize us to use their clinical data for educational purposes. Institutional review board (IRB) approval was obtained.

At the same time, a systematic literature review was conducted according to the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) guidelines.⁹ It includes only papers about GI metastasis from primary lung cancer.

Search Strategy

The research was carried out on PubMed database using the keywords: "intestinal metastasis" AND "lung cancer". The search revealed 414 published papers, dating from January 2000 to August 2017.

Studies were included in the review if present the following criteria: (1) studies that included the terms for GI metastasis from primary lung cancer; (2) they were in English or Spanish; and (3) they included adults patients only.

Studies were excluded if (1) involved animals and (2) they were systematic reviews, meta-analysis, image papers, comment papers or correspondence.

Data such as age, gender, smoking habit, lung neoplasia site, TNM, pathological histology, interval time between the lung cancer diagnosis and intestinal metastasis diagnosis, symptoms or diagnosis for hospital admission, diagnostic instrument employed, GI metastasis site, other metastasis site, GI treatment, and survival time were extracted and analyzed.

Search, data extraction and risk of bias analysis were independently performed by two authors to minimize error (A.B. and J.S.).

Statistical Analysis

Quantitative data are presented as mean±Standard Deviation (SD) and percentages. Survival analysis was performed by Kaplan–Meier method. Subgroups analysis was performed stratifying patients according to age, gender, smoking habit, tumor stage, lymph-node stage, pathological histology, synchronous vs diagnosis, clinical presentation, metastasis location and presence of extra-intestinal metastasis. A probability (P) value lower than .05 was considered statistically significant. All computations were carried out with SPSS software 22.0 (SPSS Inc., Chicago, IL, USA).

Results

Of the 414 papers identified in the search, 356 were excluded because did not meet the inclusion criteria (Fig. 1). The remaining 58 studies, published between March 2001 and August 2016, were fully analyzed and all were included in the present review, as shown in the flow diagram (Fig. 1).¹⁰⁻⁶⁷ All the papers were retrospective analysis, letters to the editor or case reports.¹⁰⁻⁶⁷

Patients' characteristics are reported in Table 1. A total of 91 patients were recruited in the present review (86 patients from the literature and 5 from the authors' series) 77 males (83.7%), 13 females (14.1%), 1 not specified gender patient. Mean age was 64.34±11.08 years, range 41–88.¹⁰⁻⁶⁷

The most common site of primary lung cancer was left upper lobe (17 patients, 18.7%), followed by right upper lobe in (16 patients, 17.6%) and right lower lobe (8

patients, 8.8%) (Table 1). Pathological histology has been reported in 78 patients (non-small cell lung cancer in 69 patients, 75.9%, small cell lung cancer in 9 patients, 9.9%). Non-small cell lung cancer was divided in: 23 adenocarcinomas (25.3%), 16 epidermoid carcinomas (17.6%), 3 sarcomatoid carcinomas (3.3%) and 2 carcinosarcomas (2.2%) (Table 1).

In 33 cases (38.8%), primary lung cancer and GI metastasis were diagnosed at the same time, and in 52 cases (61.2%) delayed. The median time between primary lung cancer diagnosis and GI metastasis diagnosis (reported in 85 cases, 93.4%) was 2 months (95% CI: 0.1–38) (Table 1).

Bowel obstruction was observed in 26 patients (28.6%; 15 intussusceptions, 10 neoplastic stenosis, 1 compression from mesenteric neoplastic infiltration), followed by GI bleeding in 25 patients (27.5%; 15 melena, 5 chronic anemia, 1 hematochezia, 1 hematemesis, 1 rectal bleeding and 2 anemia), bowel perforation in 17 patients (18.7%) and abdominal pain in 14 patients (15.4%). Five patients were asymptomatic (5.5%) and in 3 patients (3.3%) fever, perianal pain and abdominal mass were observed (Table 1).

Computed tomography (CT) scan was the most useful diagnostic test (35 patients, 38.5%) followed by endoscopy (gastroscopy, colonoscopy or enteroscopy in 15 patients, 16.5%) and laparotomy (11 patients, 12.1%) (Table 1).

The most common site of metastasis was the ileum (40 patients, 44%), followed by colon (18 patients, 19.8%) and jejunum (16 patients, 17.6%). Extra-intestinal metastasis was observed in 50 patients (54.9%) (Table 1).

Regarding treatment options, bowel resection was performed in 67 patients (73.6%), chemotherapy or radiotherapy and conservative treatment in 6 patients (6.6%), respectively, and endoscopic treatment in 2 patients (2.2%) (Table 1).

The median overall survival was 4 months (95% CI: 2.68–5.31) (Fig. 2). Survival stratified analysis revealed statistical

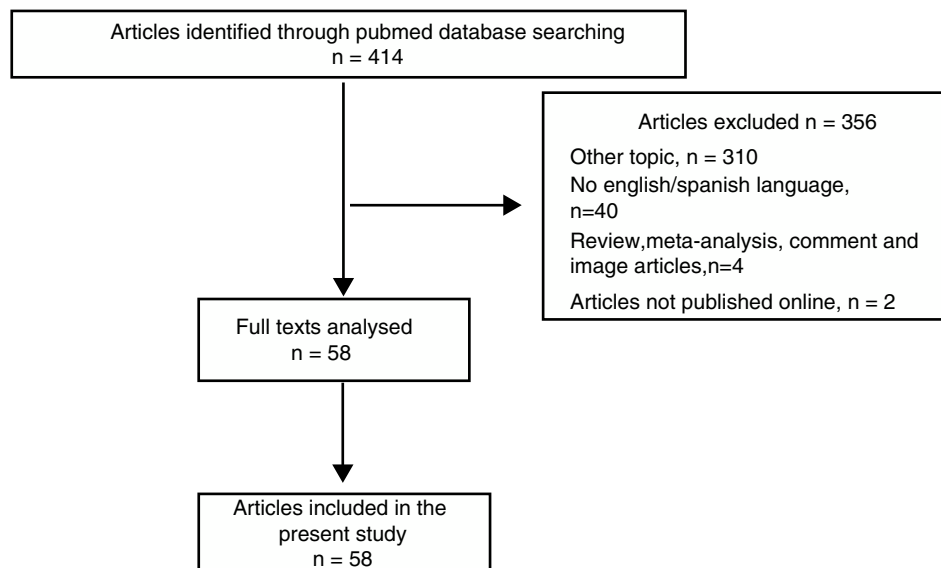


Fig. 1 – Flow diagram.

Table 1 – Patients' Characteristics.

Authors	Age (years)	Gender	Smoker	Lung neoplasia site	TNM	Pathological histology	Interval time ^a	Symptoms or diagnosis	Diagnostic instrument	GI metastasis site	Other metastasis	GI treatment	Survival	
Ise et al. ¹⁰	41	Male	N.s.	RUL	N.s.	NSCLC	9 months	Bowel perforation	Laparotomy	Jejunum	Adrenal gland, liver	Resection	1 month	
Sakorafas et al. ¹¹	36	Female	Yes	RL	N.s.	Carcinosarcoma	5 months	Bowel perforation	N.s.	Ileum	Brain	Resection	2 months	
Kim et al. ¹²	80	N.s.	N.s.	N.s.	N.s.	NSCLC	N.s.	Bowel perforation	Laparotomy	Ileum	–	Resection	2 days	
Jansen et al. ¹³	73	Female	N.s.	RUL	N.s.	NSCLC	8 months	Bleeding	Enteroscopy	Jejunum	–	Resection	Alive at 14 months	
Burnette and Ballard ¹⁴	40	Female	Yes	LUL	N.s.	NSCLC	Synchronous	Bowel perforation	CT scan	Jejunum	–	Resection	9 days	
Garwood et al. ¹⁵	54	Male	N.s.	N.s.	N.s.	Adenocarcinoma	N.s.	Bowel perforation	–	Ileum	–	Resection	21 days	
Habeşoğlu et al. ¹⁶	67	Male	Yes	RLL	T2N1M1	Epidermoid carcinoma	Synchronous	Bowel obstruction	Colonoscopy	Left colon	–	Resection	6 months	
Kanemoto et al. ¹⁷	71	Male	N.s.	RLL	N.s.	SCLC	1 months	Asymptomatic	CT scan	Ileum	Left lung, adrenal gland	Resection	36 months	
Yang et al. ¹⁸	1	71	Male	Yes	LLL	N.s.	Epidermoid carcinoma	Synchronous	Melena	Gastroscopy	Stomach	–	N.s.	4.5 months
	2	65	Male	Yes	RML	N.s.	Epidermoid carcinoma	Synchronous	Melena	Gastroscopy	Stomach	Bone, pleura	N.s.	3 months
	3	62	Male	Yes	RUL	N.s.	Adenocarcinoma	2 months	Melena	Gastroscopy	Stomach	Bone	N.s.	12.5 months
	4	50	Male	Yes	RLL	N.s.	Epidermoid carcinoma	14 months	Bowel perforation	Laparotomy	Jejunum	–	N.s.	23 days
	5	57	Male	Yes	RUL	N.s.	SCLC	2 months	Intussusception	Laparotomy	Ileum	Brain	N.s.	3 months
	6	57	Male	Yes	LUL	N.s.	SCLC	21.5 months	Hematochezia	Colonoscopy	Cecum	Brain, bone	N.s.	2 months
Kostakou et al. ¹⁹	61	Male	Yes	RLL	N.s.	NSCLC	1 months	Melena	Gastroscopy	Duodenum, jejunum	–	Blood transfusion	7 months	
Yuksel et al. ²⁰	65	Male	N.s.	N.s.	N.s.	Epidermoid Carcinoma	12 months	Bowel perforation	Laparotomy	Ileum	Brain	Resection	N.s.	
Kagohashi et al. ²¹	59	Male	Yes	LUL	N.s.	NSCLC	Synchronous	Intussusception	CT scan	Jejunum	–	Resection	6 months	

Table 1 (Continued)

Authors		Age (years)	Gender	Smoker	Lung neoplasia site	TNM	Pathological histology	Interval time ^a	Symptoms or diagnosis	Diagnostic instrument	GI metastasis site	Other metastasis	GI treatment	Survival
Karamercan et al. ²²		63	Male	N.s.	LUL	N.s.	SCLC	11 months	Abdominal pain	CT scan	Ileum	–	Resection	N.s.
Lau and Leung ²³		59	Male	Yes	LPH	N.s.	SCLC	Synchronous	Abdominal pain	Colonoscopy	Cecum	Brain	Chemotherapy	N.s.
Kim et al. ²⁴	1	79	Male	Yes	RLL	T2N0M0	N.s.	5.5 months	Abdominal pain	N.s.	Colon	–	Surgery ^a	1 month
	2	56	Male	Yes	LUL	T2N1M0	N.s.	2.5 months	Melena	N.s.	Ileum	–	Surgery ^a	69 days
	3	70	Male	Yes	LLL	T2N0M1	N.s.	1 months	Abdominal pain	N.s.	Ileum	Brain	Surgery ^a	12 days
	4	46	Female	Yes	LLL	T2N2M0	N.s.	30.5 months	Abdominal pain	N.s.	Ileum	Pleural	Surgery ^a	102 days
	5	67	Male	No	LUL	T1N1M1	N.s.	Synchronous	Abdominal pain	N.s.	Stomach	Lung	None	80 days
	6	61	Male	Yes	LUL	T3N2M0	N.s.	3.5 months	Abdominal pain	N.s.	Ileum	Adrenal gland	Surgery	Alive at 33 months
	7	72	Male	Yes	RUL	T1N0M1	N.s.	Synchronous	Asymptomatic	N.s.	Stomach	Lung, brain, adrenal gland	None	67 days
	8	78	Male	Yes	LUL	T1N3M1	N.s.	Synchronous	Hematochezia	N.s.	Colon	Lung, neck, adrenal gland, spleen	None	133 days
	9	66	Male	Yes	RLL	N.s.	N.s.	Synchronous	Hematemesis	N.s.	Stomach	Adrenal gland	Elettrocautery	145 days
	10	62	Male	Yes	RUL	T2N2M1	N.s.	Synchronous	Melena	Laparotomy	Ileum	–	Surgery	Alive at 63 months
Pollheimer et al. ²⁵		65	Female	N.s.	N.s.	N.s.	NSCLC	N.s.	Intussusception	CT scan	Ileum, cecum	–	Right hemicolectomy	N.s.
Chiu et al. ²⁶		87	Male	N.s.	RUL	N.s.	Adenocarcinoma	Synchronous	Intussusception	CT scan	Jejunum	–	Resection	3 months
Bélanger and Gagné ²⁷		60	Male	Yes	RUL, LLL	N.s.	N.s.	Synchronous	Bowel perforation	Laparoscopy	Jejunum, ileum	–	Resection	10 months
Shi et al. ²⁸		61	Male	N.s.	N.s.	T2N0M1	Sarcomatoid carcinoma	17 months	Intussusception	CT scan	Jejunum	Adrenal gland, liver, lung, brain	Resection	4 months
Meneses Grasa et al. ²⁹		69	Male	Yes	LUL	T3N2M0	Epidermoid carcinoma	6 months	Bowel obstruction	CT scan	Jejunum, ileum mesentery	–	Resection	1.5 months
Scabini et al. ³⁰		76	Male	N.s.	N.s.	N.s.	SCLC	N.s.	Bowel obstruction	–	Ileum	–	Resection	N.s.
Ara ³¹		75	Male	Yes	LPH	N.s.	Adenocarcinoma	Synchronous	Bowel obstruction	Laparotomy	Ileum	–	Resection	2.5 months

Table 1 (Continued)

Authors	Age (years)	Gender	Smoker	Lung neoplasia site	TNM	Pathological histology	Interval time ^a	Symptoms or diagnosis	Diagnostic instrument	GI metastasis site	Other metastasis	GI treatment	Survival
Weng et al. ³²	53	Male	Yes	LIL	T4N3M1	Adenocarcinoma	Synchronous	Bowel obstruction	CT scan	Colon	–	Colostomy	6 months
Kini et al. ³³	78	Male	N.s.	N.s.	N.s.	Adenocarcinoma	7 months	Abdominal pain	CT scan	Jejunum, ileum	–	Resection	Alive at 5 months
Yildirim et al. ³⁴	78	Male	N.s.	N.s.	N.s.	Epidermoid carcinoma	3 months	Abdominal pain	Laparotomy	Ileum	–	Resection	21 days
Okutur et al. ³⁵	64	Male	N.s.	LUL	N.s.	Epidermoid carcinoma	4 months	Rectal bleeding	Rectal examination	Anal canal	–	Radiotherapy	N.s.
Otera et al. ³⁶	63	Male	Yes	N.s.	N.s.	NSCLC	Synchronous	Intussusception	CT scan	Ileum	–	Resection	27 days
Akamatsu et al. ³⁷	72	Male	Yes	RUL	N.s.	NSCLC	Synchronous	Asymptomatic	CT scan	Jejunum	–	Chemotherapy	5 months
Lin et al. ³⁸	76	Male	No	LUL	N.s.	Adenocarcinoma	0.5 months	Melena	Gastroscopy	Duodenum	Bone	Blood transfusion	2.5 months
Papaziogas et al. ³⁹	68	Male	Yes	RLL	N.s.	Epidermoid carcinoma	8 months	Bowel obstruction	CT scan	Ileum	–	Resection	4 months
Yamada et al. ⁴⁰	66	Male	Yes	LUL	T4N3M1	Epidermoid carcinoma	Synchronous	Bowel perforation	CT scan	Duodenum, ileum	–	Resection	4 months
Nishizawa et al. ⁴¹	1 55	Male	N.s.	N.s.	T1N0	Adenocarcinoma	Synchronous	Bowel perforation	Abdominal X-ray	Ileum	Liver, brain	Resection	53 days
	2 58	Male	N.s.	N.s.	T4N1	Adenocarcinoma	17.4 months	Bowel perforation	Abdominal X-ray	Jejunum	Colon	Resection	108 days
	3 40	Male	N.s.	N.s.	T2N3	Adenocarcinoma	6.7 months	Bowel perforation	Abdominal X-ray	Ileum	Brain	Resection	347 days
	4 56	Male	N.s.	N.s.	T2N3	Adenocarcinoma	9.1 months	Abdominal pain	Gastroscopy	Duodenum	Liver	Bypass	25 days
	5 78	Male	N.s.	N.s.	T4N2	Epidermoid carcinoma	2.3 months	Bowel perforation	CT scan	Ileum	Lung, liver, bone, adrenal gland	Resection	67 days
	6 62	Male	N.s.	RUL	T1N0	Adenocarcinoma	14.7 months	Abdominal pain	Gastroscopy	Jejunum	–	Resection	742 days
	7 68	Male	N.s.	N.s.	T4N1	Adenocarcinoma	31.3 months	Abdominal pain	CT scan	Ileum	Brain, bone	Bypass	302 days
Fujiwara et al. ⁴²	1 66	Female	N.s.	N.s.	N.s.	NSCLC	6.7 months	Melena	N.s.	Colon	–	Resection	40 months
	2 68	Male	N.s.	N.s.	N.s.	NSCLC	9.5 months	Anemia	N.s.	Ileum	–	Resection	93.6 months
	3 70	Female	N.s.	N.s.	N.s.	NSCLC	19.5 months	Melena	N.s.	Rectum	–	Resection	46.9 months
	4 48	Male	N.s.	N.s.	N.s.	NSCLC	9.4 months	Melena	N.s.	Ileum	Adrenal gland	Resection	14.9 months

Table 1 (Continued)

Authors		Age (years)	Gender	Smoker	Lung neoplasia site	TNM	Pathological histology	Interval time ^a	Symptoms or diagnosis	Diagnostic instrument	GI metastasis site	Other metastasis	GI treatment	Survival
	5	83	Male	N.s.	N.s.	N.s.	NSCLC	6.9 months	Abdominal mass	N.s.	Colon	Liver	Resection	3.7 months
	6	51	Male	N.s.	N.s.	N.s.	NSCLC	2.2 months	Anemia	N.s.	Stomach	Skin, brain	N.s.	0.4 months
	7	57	Male	N.s.	N.s.	N.s.	NSCLC	1.2 months	Anemia, ileus	N.s.	Ileum, stomach	Liver, kidney	N.s.	1.1 months
	8	69	Male	N.s.	N.s.	N.s.	NSCLC	14.3 months	N.s.	N.s.	Colon	Adrenal gland, brain	N.s.	0.2 months
	9	70	Male	N.s.	N.s.	N.s.	N.s.	4 months	Melena	N.s.	Ileum	Adrenal gland, pancreas	N.s.	10.8 months
Tanaka et al. ⁴³	85	Male	N.s.	N.s.	T4N1M1	Epidermoid carcinoma	120 months	Bowel perforation	CT scan	Jejunum	Bone	Resection		3 months
Song et al. ⁴⁴	58	Male	N.s.	LUL	N.s.	NSCLC	Synchronous	Bowel obstruction	CT scan	Jejunum	Bladder, adrenal gland, brain	Resection		N.s.
Jarmin et al. ⁴⁵	75	Male	N.s.	N.s.	N.s.	SCLC	Synchronous	Intussusception	Laparotomy	Duodenum, jejunum	N.s.	Whipple's procedure, resection		N.s.
Guner et al. ⁴⁶	71	Male	N.s.	N.s.	T3N1	Sarcomatoid carcinoma	N.s.	Intussusception	Laparotomy	Ileum	N.s.	Resection		9 months
Parejo- Sánchez et al. ⁴⁷	60	Male	Yes	N.s.	T1N0M0	NSCLC	15	Bleeding	Laparotomy	Jejunum	–	Resection		N.s.
Li Destri et al. ⁴⁸	73	Male	N.s.	N.s.	N.s.	Neuroendocrine carcinoma	Synchronous	Bowel obstruction	CT scan	Ileum	Brain	Resection		277 days
Lin et al. ⁴⁹	78	Male	Yes	RUL	N.s.	NSCLC	Synchronous	Intussusception	CT scan	Jejunum, colon	–	Resection		3 months
Hara et al. ⁵⁰	58	Male	N.s.	RUL	T2N0M0	NSCLC	9 months	Fever	CT scan	Ileum	–	Resection		4 months
Rivera et al. ⁵¹	61	Female	Yes	RUL	N.s.	Adenocarcinoma	Synchronous	Abdominal pain	CT scan	Ileum	Mediastinum, left supraclavicular space	Resection		Alive at 5 months

Table 1 (Continued)

Authors	Age (years)	Gender	Smoker	Lung neoplasia site	TNM	Pathological histology	Interval time ^a	Symptoms or diagnosis	Diagnostic instrument	GI metastasis site	Other metastasis	GI treatment	Survival
Koh et al. ⁵²	46	Male	Yes	RUL	N.s.	NSCLC	0.3 moths	Bowel perforation	CT scan	Ileum	Stomach, duodenum, kidneys, pancreas, gallbladder, adrenal gland, thyroid	Resection	14 days
Khan et al. ⁵³	60	Male	Yes	RUL	N.s.	SCLC	Synchronous	Anemia	Colonoscopy	Cecum	Brain, liver, spleen	Polypectomy	11 months
Sifuentes Giraldo et al. ⁵⁴	73	Male	Yes	LUL	N.s.	Adenocarcinoma	Synchronous	Bowel perforation	CT scan	Colon	-	Resection	2 months
de Miguel Valencia et al. ⁵⁵	48	Male	Yes	LIL	N.s.	Sarcomatoid carcinoma	Synchronous	Intussusception	CT scan	Ileum	Lung, bone, cerebral, adrenal gland	Resection	5 months
Guerra et al. ⁵⁶	75	Female	Yes	N.s.	N.s.	SCLC	1 months	Perianal pain	Rectal examination	Rectum	Bone	Chemotherapy	Alive at 7 months
Mandeville et al. ⁵⁷	49	Female	N.s.	LUL	T4N0M1b	NSCLC	Synchronous	Intussusception	Laparoscopy	Ileum	Bone, brain	Resection	6 months
Liu et al. ⁵⁸	66	Male	N.s.	RLL	T2N1M0	Epidermoid carcinoma	8 months	Melena	CT scan	Ileum	-	Resection	Alive at 5 months
Lu et al. ⁵⁹	62	Female	N.s.	N.s.	N.s.	Adenocarcinoma	Synchronous	Melena	Colonoscopy	Colon	Skin	Chemotherapy	Alive at 2 months
Lu et al. ⁶⁰	78	Male	Yes	N.s.	TxN1M1	Adenocarcinoma	4 months	Melena	CT scan	Jejunum	Adrenal gland, bone	Resection	2 months
Chen ⁶¹	61	Male	Yes	RPH	N.s.	Adenocarcinoma	Synchronous	Intussusception	CT scan	Ileum	-	Resection	Alive at 3 months
Escoda ⁶²	63	Male	N.s.	LPH	N.s.	Epidermoid carcinoma	Synchronous	Bowel obstruction	CT scan	Ileum	Myocardium, bone	Resection	-
Romano et al. ⁶³	60	Male	Yes	LIL	N.s.	Carcinosarcoma	0.5 moths	Intussusception	CT scan	Ileum	Liver, omentum	Resection	8 days
Nunes et al. ⁶⁴	43	Male	Yes	RUL	T2N0M1	Adenosquamous carcinoma	Synchronous	Bowel obstruction	Colonoscopy	Left colon, duodenum	Brain	Resection	Alive at 18 months

Table 1 (Continued)

Authors	Age (years)	Gender	Smoker	Lung neoplasia site	TNM	Pathological histology	Interval time ^a	Symptoms or diagnosis	Diagnostic instrument	GI metastasis site	Other metastasis	GI treatment	Survival	
Iwamuro et al. ⁶⁵	71	Male	N.s.	RML	T3N2M1	Adenocarcinoma	N.s.	Melena	Gastroscopy	Duodenum	Adrenal gland	Chemotherapy	5 months	
Nakamura et al. ⁶⁶	88	Female	N.s.	N.s.	T1N1M0	Epidermoid carcinoma	144 months	Intussusception	CT scan	Ileum	–	Resection	5 months	
Fujii et al. ⁶⁷	55	Female	N.s.	LUL	N.s.	NSCLC	Synchronous	Intussusception	CT scan	Jejunum	–	Resection	Alive at 11 months	
Present series	1	69	Male	Yes	LPH	T4N3M1	Epidermoid carcinoma	6 months	Bowel obstruction	CT scan	Ileum	Liver, bone, peritoneum, mesentery	Resection	1.5 months
	2	79	Male	Yes	RML	T4N2M1	Adenocarcinoma	Synchronous	Bowel perforation	CT scan	Jejunum	Peritoneum	Resection	1 months
	3	67	Male	Yes	LUL	T4N2M1	Adenocarcinoma	5.5 months	Bowel perforation	CT scan	Ileum	Adrenal gland, abdominal wall	Resection	1 months
	4	53	Male	Yes	LIL	T1N2M1	NSCLC	7 months	Abdominal pain	Entero-MRI	Jejunum, ileum	Liver, spleen, vertebrae	Conservative	8 months
	5	72	Male	Yes	RUL	T3N0M0	Adenocarcinoma	12 months	Asymptomatic	PET-CT	Ileum	Brain	Resection	4 months

^a Interval time between the lung cancer diagnosis and intestinal metastasis diagnosis. GI: Gastrointestinal. a: surgical procedure not specified. NSCLC: non-small cell lung carcinoma. SCLC: small cell lung carcinoma. N.s.: not specified. CT: computed tomography. MRI: magnetic resonance imaging. PET: positron emission tomography. RL: right lobe. RPH: right pulmonary hilum. RUL: right upper lobe. RML: right middle lobe. RLL: right lower lobe. LPH: left pulmonary hilum. LUL: left upper lobe. LIL: left inferior lobe. LLL: left lingual lobe.

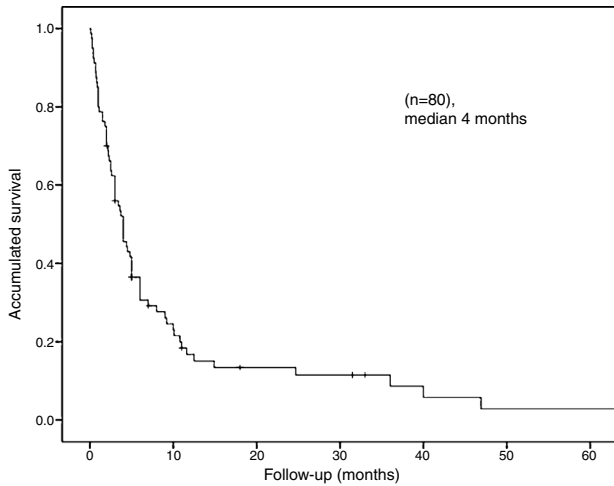


Fig. 2 – Kaplan-Meier plot of the overall survival curve.

significant differences when the patients were compared according to gender (male vs female: 3.7 months, 95% CI: 2.7–4.6 vs 6 months, 95% CI: 0–36.5, Log-rank: $P=.01$), age (<70 vs ≥ 70 : 4 months, 95% CI: 2.4–5.5 vs 3 months, 95% CI: 2.1–3.8, Log-rank: $P=.04$), clinical presentation (bowel perforation vs

others: 1.8 months. 95% CI: 0.4–3.1 vs 4.8 months, 95% CI: 3.9–5.6, Log-rank: $P=.0001$) and metastasis location (colon-rectum vs small bowel vs stomach: 6 months, 95% CI: 3.3–86 vs 4 months, 95% CI: 3–4.9 vs 2.6 months, 95% CI: 1.6–3.5, Log-rank: $P=.03$) (Fig. 3). No statistically significant differences were observed when patients were stratified according smoking habit, pathological histology, tumor stage, lymph-node stage, presence of extra-intestinal metastasis and synchronous vs delay diagnosis.

Discussion

From March 2001 to August 2017, 86 cases of GI metastasis from primary lung cancer are reported in literature^{10–67} and between 2012 and 2017, in authors' hospital, 5 patients were treated for the same reason, for a total of 91 patients included in the present study. The treatment of choice of this type of lesions, is still debated in literature, due to the lack of reported large series and the difficulty to perform Randomized Control Trials (RCTs) due to the patients' heterogeneous characteristics who experience GI metastasis. Often, the treatment is affected by patients' urgency conditions, such as bowel perforation or obstruction and bleeding, that do not allow to choose a different treatment than surgery. For these reasons

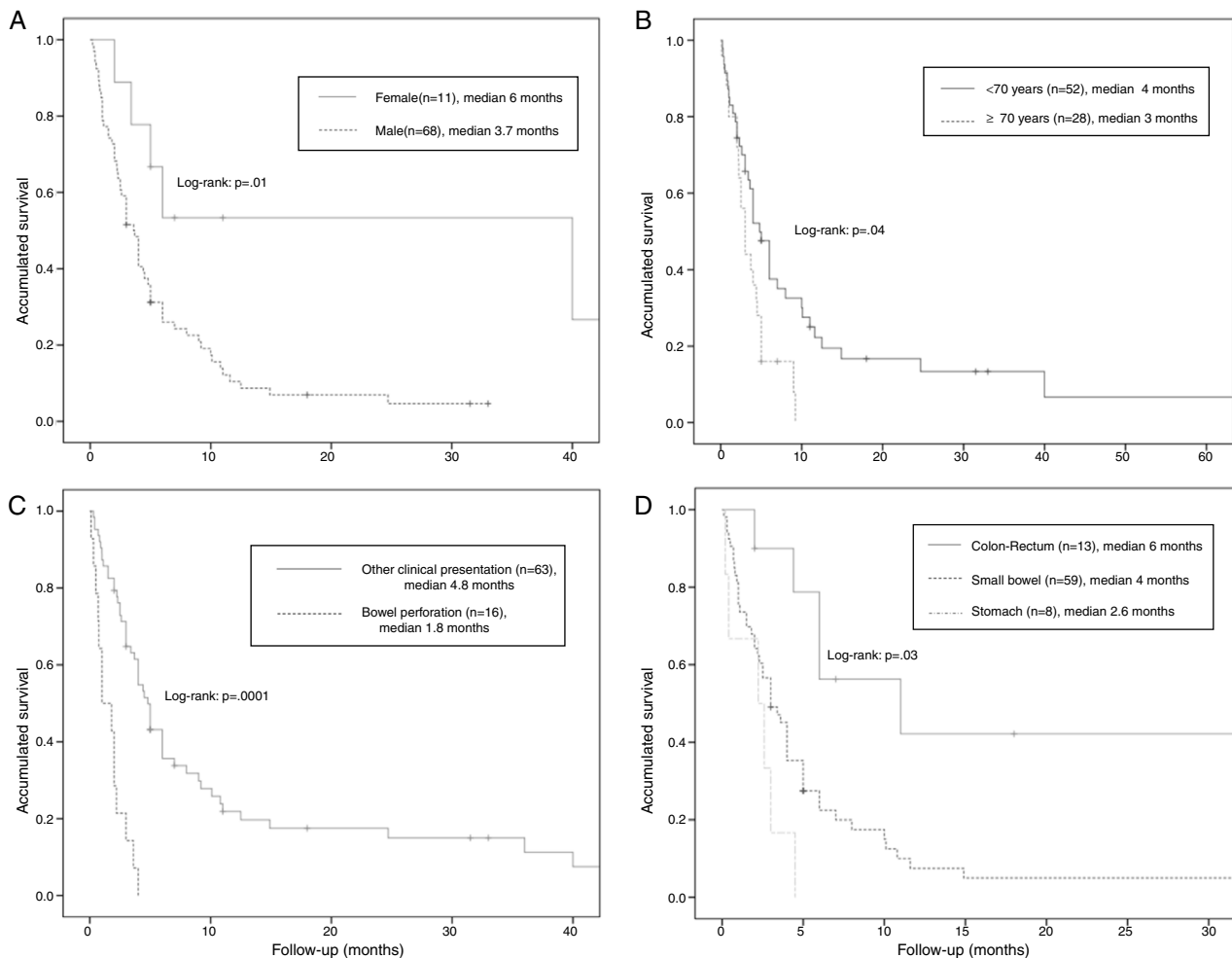


Fig. 3 – Kaplan-Meier plot of the survival curve based on gender (A), age (B), clinical presentation (C) and metastasis location (D).

and due to the patients' poor condition at the time of GI metastasis diagnosis (advanced stage cancer, old age, severe symptoms) the median survival rate is very low.⁷

We have investigated with the aim to analyze our data and those reporting in literature regarding GI metastasis from primary lung cancer. Anyway, the present study has several biases, such as the relative small number of patients and several missing data from the literature.

The most frequent lung histological subtype cancer related to GI metastasis is still debated in literature^{3,5,7,8,24} but in the present series, Large cell carcinoma is the most common observed (75.9%).

The majority of patients with GI metastasis from a primary lung cancer are asymptomatic,⁵ as evidenced by the discrepancy between the estimated incidence in clinical studies and post-mortem studies.²⁴ This clinical under-diagnosis may be due to the fact that the GI discomfort, referred by these patients, is often confused with chemotherapy side effects⁶⁸ and for this reason requires a greater degree of suspicion by the clinician for early identification. The most frequent uncomplicated symptoms observed are the abdominal pain occurred in 50% of patients and weight loss.^{7,69} Among complicated symptoms, small bowel perforation is described,^{7,70} such as the obstruction that can occur as a consequence of an occlusive mass²⁴ or by intussusception of the affected ileal tract.^{7,33} Finally, acute digestive hemorrhage may be observed as melena in case of stomach, duodenum or small bowel lesions⁷¹ and rectal bleeding in case of lower GI tract involvement.⁶⁸ In the present series, small bowel obstruction is the most frequent complicated symptom observed (28.6%) as well as reported by Di et al. (35%).⁷

Lung metastasis can be observed in all GI tract such as esophagus (6.3%), small bowel (2.6%), stomach (1.2%) and colon (0.7%).³ Based on the literature, the most frequent small bowel site are the jejunum and ileum,^{7,24,72} while the duodenum is usually affected in a smaller number of cases.⁷³ In the present series, the most frequent metastasis site is in the ileum (44%).

CT scan is the most used diagnostic test, both in authors' experience and in the literature.⁵ This test has been widely described⁵ due to its versatility and easy access in the context of urgency, with an estimated sensitivity rate of 72%,⁷⁴ however, it has been shown difficulty in detecting small lesions.⁷⁴ Positron emission tomography-CT (PET-CT) scan shown to be useful in the diagnosis of metastasis from primary lung cancer also in case of asymptomatic GI metastasis.^{75,76} Although, in the present study is employed only in one patient, and, at now, no sufficient data about sensitivity and specificity of this test are available.⁷⁷ The use of endoscopic approach has been described in several series as a diagnostic test in patients who present digestive bleeding or anemia.^{68,69,76,77} A recent study reports the use of endoscopic capsule such as feasible diagnostic test for small bowel lesions and as a non-invasive diagnostic method that could reduce the metastasis under-diagnosis.⁷⁸ Magnetic resonance imaging (MRI) is a less common diagnostic test proposed in the literature,⁴⁷ and has been employed in only one patient of the present series.

The treatment of choice of the lung GI metastasis is still debated in literature, between authors that support conservative approach^{8,79} and authors in favor of surgical approach.^{3,24} Anyway, in case of bowel perforation or obstruction or in case of massive bleeding, the surgical approach is often the only possible treatment.³ A perioperative mortality rate between 20% and 100%, is reported in literature, in patients who underwent surgery^{8,79} but it should be noted that most of these deaths were not due to immediate surgical complications.⁷ Goh et al. suggest that an adequate selection of patients who underwent surgery could increase the survival rate,³ considering multiple extra-intestinal metastasis and bowel perforation the most important factors that affected the postoperative outcomes.³ In the present series perioperative mortality was observed in one case. The most common surgical technique performed, in the literature such as in the present series, is the bowel resection with primary anastomosis by laparotomy,^{3,8} but a recent study shows the feasibility of laparoscopic approach.⁸⁰

The median survival ranges between 1 and 6 months.^{3,7,8,24} The largest series published in literature, that reports a retrospective analysis of 100 previously published cases (including autopsies), shows a median survival of 2.3 months⁷ and reports that the risk factors mostly associated with mortality are: age greater than 70 years, bowel perforation and presence of extra-intestinal metastasis,⁷ as well as confirmed in this series. In the present study, the survival rate is similar to that published in literature (4 months, 95% CI: 2.68-5.31), and stratifying the patients, the statistical significant differences were observed only for gender, age, clinical presentations and metastasis site.

The gold standard treatment is not still available based on the published data, and none of the reported treatments had a significant impact on survival. Anyway, surgical treatment cannot defer in case of bowel perforation but also in some case of massive bleeding or bowel obstruction. For this reason, in patients with acute abdomen and history of lung cancer, GI metastasis should be considered such as differential diagnosis. At the time of primary lung cancer diagnosis, after CT scan, PET-CT scan could be helpful to diagnose eventual synchronous metastasis.

To the best of the authors' knowledge, this is the first systematic review, concerning GI metastasis from primary lung cancer, reported in literature.

Randomized clinical trials are difficult to perform due to the rarity and the heterogeneity of these lesions, however a wider sample size of patients, and further studies are required to confirm these data.

Authors' Contribution

Andrea Balla: study designs, acquisition of data, analysis and interpretation of results, manuscript preparation, critical revision and approval of the final version of the manuscript.

José D. Subiela: study designs, acquisition of data, analysis and interpretation of results, manuscript preparation, critical revision and approval of the final version of the manuscript.

Jesús Bollo: study designs, acquisition of data, analysis and interpretation of results, manuscript preparation, critical revision and approval of the final version of the manuscript.

Carmen Martínez: analysis and interpretation of results, manuscript preparation, critical revision and approval of the final version of the manuscript.

Carlos Rodríguez Luppi: analysis and interpretation of results, manuscript preparation, critical revision and approval of the final version of the manuscript.

Pilar Hernández: analysis and interpretation of results, manuscript preparation, critical revision and approval of the final version of the manuscript.

Yuliana Pascual: analysis and interpretation of results, manuscript preparation, critical revision and approval of the final version of the manuscript.

Silvia Quaresima: analysis and interpretation of results, manuscript preparation, critical revision and approval of the final version of the manuscript.

Eduard M. Targarona: study designs, acquisition of data, analysis and interpretation of results, manuscript preparation, critical revision and approval of the final version of the manuscript.

Conflict of Interest

Dr. Andrea Balla, Dr. José D. Subiela, Dr. Jesús Bollo, Dr. Carmen Martínez, Dr. Carlos Rodríguez Luppi, Dr. Pilar Hernández, Dr. Yuliana Pascual, Dr. Silvia Quaresima and Professor Eduard M. Targarona have no conflicts of interest or financial ties to disclose.

REFERENCES

- Ridge CA, McErlean AM, Ginsberg MS. Epidemiology of lung cancer. *Semin Intervent Radiol*. 2013;30:93-8. <http://dx.doi.org/10.1055/s-0033-1342949>.
- Park JY, Jang SH. Epidemiology of lung cancer in Korea: recent trends. *Tuberc Respir Dis (Seoul)*. 2016;79:58-69. <http://dx.doi.org/10.4046/trd.2016.79.2.58>.
- Goh BK, Yeo AW, Koong HN, Ooi LL, Wong WK. Laparotomy for acute complications of gastrointestinal metastases from lung cancer: is it a worthwhile or futile effort? *Surg Today*. 2007;37:370-4.
- Malik PS, Raina V. Lung cancer: prevalent trends & emerging concepts. *Indian J Med Res*. 2015;141:5-7.
- Jevremovic V. Is gastrointestinal metastasis of primary lung malignancy as rare as reported in the literature? A comparison between clinical cases and post-mortem. *Stud Oncol Hematol Rev*. 2016;12:51-7. <http://dx.doi.org/10.17925/OHR.2016.12.01.51>.
- Yoshimoto A, Kasahara K, Kawashima A. Gastrointestinal metastases from primary lung cancer. *Eur J Cancer*. 2006;42:3157-60.
- Di JZ, Peng JY, Wang ZG. Prevalence, clinicopathological characteristics, treatment, and prognosis of intestinal metastasis of primary lung cancer: a comprehensive review. *Surg Oncol*. 2014;23:72-80. <http://dx.doi.org/10.1016/j.suronc.2014.02.004>.
- Lee PC, Lo C, Lin MT, Liang JT, Lin BR. Role of surgical intervention in managing gastrointestinal metastases from lung cancer. *World J Gastroenterol*. 2011;17:4314-20. <http://dx.doi.org/10.3748/wjg.v17.i38.4314>.
- Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA*. 2000;283:2008-12.
- Ise N, Kotanagi H, Morii M, Yasui O, Ito M, Koyama K, et al. Small bowel perforation caused by metastasis from an extra-abdominal malignancy: report of 3 cases. *Surg Today*. 2001;31:358-62.
- Sakorafas GH, Pavlakis G, Grigoriadis KD. Small bowel perforation secondary to metastatic lung cancer: a case report and review of the literature. *Mt Sinai J Med*. 2003;70:130-2.
- Kim DY, Joo JK, Ryu SY, Kim YJ, Kim SK, Juhng SW. Metastatic anaplastic carcinoma of the small intestine arising from the lung. *Cancer Res Treat*. 2003;35:364-6. <http://dx.doi.org/10.4143/crt.2003.35.4.364>.
- Jansen JM, Oldenburg B, van Milligen de Wit AW. Small intestinal metastasis from non-small-cell carcinoma of the lung: a rare cause of GI bleeding of obscure origin. *Gastrointest Endosc*. 2004;59:447-9.
- Burnette RE, Ballard BR. Metastatic pleomorphic carcinoma of lung presenting as abdominal pain. *J Natl Med Assoc*. 2004;96:1657-60.
- Garwood RA, Sawyer MD, Ledesma EJ, Foley E, Claridge JA. A case and review of bowel perforation secondary to metastatic lung cancer. *Am Surg*. 2005;71:110-6.
- Habeşoğlu MA, Oğuzülgen KI, Öztürk C, Akyürek N, Memiş L. A case of bronchogenic carcinoma presenting with acute abdomen. *Tuberk Toraks*. 2005;53:280-3.
- Kanemoto K, Kurishima K, Ishikawa H, Shiotani S, Satoh H, Ohtsuka M. Small intestinal metastasis from small cell lung cancer. *Intern Med*. 2006;45:967-70.
- Yang CJ, Hwang JJ, Kang WY, Chong IW, Wang TH, Sheu CC, et al. Gastro-intestinal metastasis of primary lung carcinoma: clinical presentations and outcome. *Lung Cancer*. 2006;54:319-23.
- Kostakou C, Khaldi L, Flossos A, Kapsoritakis AN, Potamianos SP. Melena: a rare complication of duodenal metastases from primary carcinoma of the lung. *World J Gastroenterol*. 2007;13:1282-5.
- Yuksel O, Uyar P, Sahin TT, Demirhan B. Small bowel perforation due to metastatic lung squamous cell carcinoma. *Saudi Med J*. 2007;28:631-3.
- Kagohashi K, Kadono K, Satoh H, Ohtsuka M. Intussusception due to intestinal metastasis from lung cancer. *Lung Cancer*. 2007;57:247-8.
- Karamercan A, Bostancı H, Aytac B. A small bowel fistula extending into a metastatic tumour due to lung carcinoma. *Acta Chir Belg*. 2007;107:436-7.
- Lau CP, Leung WK. Caecal metastasis from a primary small-cell lung carcinoma. *Hong Kong Med J*. 2008;14:152-3.
- Kim MS, Kook EH, Ahn SH, Jeon SY, Yoon JH, Han MS, et al. Gastrointestinal metastasis of lung cancer with special emphasis on a long-term survivor after operation. *J Cancer Res Clin Oncol*. 2009;135:297-301. <http://dx.doi.org/10.1007/s00432-008-0424-0>.
- Pollheimer MJ, Eberl T, Baumgartner K, Pollheimer VS, Tschmelitsch J, Lackner H, et al. Ileocecal intussusception caused by lung cancer metastasis. *Wien Klin Wochenschr*. 2009;121:413-6. <http://dx.doi.org/10.1007/s00508-009-1146-2>.
- Chiu WK, Lin YC, Wang LT, Chen JH, Yu JC, Hsieh CB. Jejunojejunal intussusception secondary to metastasis from adenocarcinoma of the lung — a case report. *Acta Chir Belg*. 2009;109:519-22.

27. Bélanger M, Gagné JP. Mock appendicitis: small bowel perforation secondary to lung cancer metastasis. *Can J Surg*. 2009;52:E205-6.
28. Shi B, Gaebelein G, Hildebrandt B, Weichert W, Glanemann M. Adult jejunojejunal intussusception caused by metastasized pleomorphic carcinoma of the lung: report of a case. *Surg Today*. 2009;39:984-9. <http://dx.doi.org/10.1007/s00595-008-3954-9>.
29. Meneses Grasa Z, Coll Salinas A, Macías Cerrolaza JA, Aguayo Albasini JL, Campillo Soto A, Guillén Paredes MP. Intestinal obstruction by metastasis in mesentery from squamous cell lung carcinoma. *Rev Esp Enferm Dig*. 2009;101:817-8.
30. Scabini S, Rimini E, Romairone E, Scordamaglia R, Boggio M, Musizzano Y, et al. Small bowel metastasis from primary neuroendocrine small cell lung carcinoma. *Chir Ital*. 2009;61:679-82.
31. Ara C, Dirican A, Ozgör D, Pişkin T. A case of acute small bowel obstruction due to metastasis of undiagnosed primary carcinoma of the lung. *Turk J Gastroenterol*. 2009;20:302-3.
32. Weng MW, Wang HC, Chiou JC, Lin SL, Lai RS. Colonic metastasis from a primary adenocarcinoma of the lung presenting with acute abdominal pain: a case report. *Kaohsiung J Med Sci*. 2010;26:40-4. [http://dx.doi.org/10.1016/S1607-551X\(10\)70007-3](http://dx.doi.org/10.1016/S1607-551X(10)70007-3).
33. Kini S, Kapadia RM, Amarapurkar A. Intussusception due to intestinal metastasis from lung cancer. *Indian J Pathol Microbiol*. 2010;53:141-3. <http://dx.doi.org/10.4103/0377-4929.59208>.
34. Yildirim M, Tasli F, Bayam ME, Postaci H. A rare cause of small bowel transection: metastatic lung cancer. *Med Princ Pract*. 2010;19:232-4. <http://dx.doi.org/10.1159/000285300>.
35. Okutur K, Arslan K, Bozkurt M, Barlan M, Oz B, Demir G. Squamous cell carcinoma of the lung with anal canal metastasis. *J BUON*. 2010;15:194.
36. Otera H, Ikeda F, Nakagawa S, Kono Y, Sakurai T, Tada K, et al. Intussusception of small intestine due to metastasis of large cell carcinoma of the lung with a rhabdoid phenotype. *Eur Respir Rev*. 2010;19:248-52. <http://dx.doi.org/10.1183/09059180.00001610>.
37. Akamatsu H, Tsuya A, Kaira K, Nakamura Y, Naito T, Murakami H, et al. Intestinal metastasis from non-small-cell lung cancer initially detected by ¹⁸F-fluorodeoxyglucose positron emission tomography. *Jpn J Radiol*. 2010;28:684-7.
38. Lin HC, Yu CP, Lin HA, Lee HS. A case of lung cancer metastasized to the gastrointestinal anastomosis site where the primary gastric cancer was resected 17 years ago. *Lung Cancer*. 2011;72:255-7. <http://dx.doi.org/10.1016/j.lungcan.2011.02.005>.
39. Papaziogas B, Koutelidakis I, Christopoulos P, Doulias T, Paraskevas G, Atmatzidis S, et al. Intestinal metastasis of a primary lung carcinoma presenting as mechanical small bowel obstruction. *J Gastrointest Cancer*. 2012;43 Suppl. 1:S13-5. <http://dx.doi.org/10.1007/s12029-011-9297-6>.
40. Yamada H, Akahane T, Horiuchi A, Shimada R, Shibuya H, Hayama T, et al. A case of lung squamous cell carcinoma with metastases to the duodenum and small intestine. *Int Surg*. 2011;96:176-81.
41. Nishizawa Y, Kobayashi A, Saito N, Nagai K, Sugito M, Ito M, et al. Surgical management of small bowel metastases from primary carcinoma of the lung. *Surg Today*. 2012;42:233-7. <http://dx.doi.org/10.1007/s00595-011-0005-8>.
42. Fujiwara A, Okami J, Tokunaga T, Maeda J, Higashiyama M, Kodama K. Surgical treatment for gastrointestinal metastasis of non-small-cell lung cancer after pulmonary resection. *Gen Thorac Cardiovasc Surg*. 2011;59:748-52. <http://dx.doi.org/10.1007/s11748-011-0811-3>.
43. Tanaka T, Minami S, Tsutsumi R, Azuma T, Matsuo S, Abe K, et al. A metastatic jejunal tumor from squamous cell carcinoma of the lung found in an intestinal perforation. *Case Rep Gastroenterol*. 2011;5:636-41. <http://dx.doi.org/10.1159/000334426>.
44. Song Y, Li M, Shan J, Ye X, Tang S, Fang X, et al. Acute small bowel obstruction: a rare initial presentation for the metastasis of the large-cell carcinoma of the lung. *World J Surg Oncol*. 2012;10:26. <http://dx.doi.org/10.1186/1477-7819-10-26>.
45. Jarmin R, Azman A, Rahim R, Kosai NR, Das S. A rare case of intussusception associated with metastasized small cell carcinoma of lung. *Acta Med Iran*. 2012;50:782-4.
46. Guner A, Karyagar S, Livaoglu A, Kece C, Kucuktulu U. Small bowel intussusception due to metastasized sarcomatoid carcinoma of the lung: a rare cause of intestinal obstruction in adults. *Case Rep Surg*. 2012;2012:962683. <http://dx.doi.org/10.1155/2012/962683>.
47. Parejo-Sánchez MI, Pardo-Cabello AJ, Martínez-Ceres M, Sánchez-Ramos C. Single intestinal metastasis of non-small cell lung carcinoma. *Rev Esp Enferm Dig*. 2013;105:55-6.
48. Li Destri G, Ferraro MJ, Vecchio G, Musumeci A, Calabrin M, Giarrizzo A. Primary neuroendocrine lung tumor presenting with acute ileal obstruction. *Case report. G Chir*. 2013;34:78-81.
49. Lin MW, Wu CT, Chang YL. Intussusception caused by intestinal metastasis from lung pleomorphic carcinoma. *Ann Thorac Cardiovasc Surg*. 2014;20 Suppl.:635-8. <http://dx.doi.org/10.5761/atcs.cr.13-00099>.
50. Hara S, Hosoi K, Suga Y, Takata T, Degami H, Kinoshita Y, et al. Multiple cytokines-producing pleomorphic carcinoma of lung with metastasis to the small intestine. *Ann Thorac Cardiovasc Surg*. 2014;20 Suppl.:666-8. <http://dx.doi.org/10.5761/atcs.cr.13-00202>.
51. Rivera NT, Katz H, Weisbaum G, Guarneri R, Bray N, Constanza-Guaqueta D. Solitary metastasis to the small bowel from primary adenocarcinoma of the lung. *J Gastrointest Cancer*. 2014;45 Suppl. 1:91-5. <http://dx.doi.org/10.1007/s12029-013-9567-6>.
52. Koh H, Chiyotani A, Tokuda T, Suzumura H, Kamiishi N, Takahashi H, et al. Pleomorphic carcinoma showing rapid growth, multiple metastases, and intestinal perforation. *Ann Thorac Cardiovasc Surg*. 2014;20 Suppl.:669-73. <http://dx.doi.org/10.5761/atcs.cr.13-00167>.
53. Khan AM, Khan S, Dave V, Bhargri H. Small cell lung carcinoma presenting as a caecal polyp on surveillance colonoscopy. *BMJ Case Rep*. 2014;2014. <http://dx.doi.org/10.1136/bcr-2013-202624>. pii:bcr2013202624.
54. Sifuentes Giraldo WA, González García A, Chamorro Tojeiro S, Sánchez Sánchez O, Pian H, Vázquez Díaz M. Colonic perforation secondary to metastatic lung adenocarcinoma during anti-TNF treatment for ankylosing spondylitis. *Acta Reumatol Port*. 2014;39:72-6.
55. De Miguel Valencia M, Esquíroz Lizaur I, Marzo Virto J, de Miguel Velasco M, Yagüe Hernando A. Intestinal intussusception as the first manifestation of lung cancer. *An Sist Sanit Navar*. 2014;37:299-304.
56. Guerra F, Amore Bonapasta S, Tumbiolo S, Gentile E, Coratti A. Lung cancer metastasis to the external anal sphincter mimicking perianal abscess. *Int J Colorectal Dis*. 2015;30:581-2. <http://dx.doi.org/10.1007/s00384-014-2032-6>.
57. Mandeville Y, de Gheldere C, Vanclooster P. Small bowel intussusception caused by multiple intestinal metastases from a giant cell carcinoma of the lung: a case report. *Acta Chir Belg*. 2015;115:49-51. <http://dx.doi.org/10.1080/00015458.2015.11681066>.
58. Liu W, Zhou W, Qi WL, Ma YD, Xu YY. Gastrointestinal hemorrhage due to ileal metastasis from primary lung

- cancer. *World J Gastroenterol.* 2015;21:3435-40. <http://dx.doi.org/10.3748/wjg.v21.i11.3435>.
59. Lu S, Yang J, Sun Y, Xu Z. Multiple cutaneous and intestinal metastases in lung cancer: a case report. *Oncol Lett.* 2015;9:1541-4.
 60. Lu B, Ding C, Wang C, Cao J. A case of small intestinal hemorrhage secondary to metastatic lung cancer in the elderly. *Chin J Cancer Res.* 2015;27:218-20. <http://dx.doi.org/10.3978/j.issn.1000-9604.2014.11.01>.
 61. Chen J. Undiagnosed primary lung carcinoma with initial manifestation of intestinal obstruction: a case report and literature review. *J Cancer Res Ther.* 2015;11 Suppl. 1:C134-7. <http://dx.doi.org/10.4103/0973-1482.163873>.
 62. Escoda AP. Metastatic obstruction of the small bowel revealing squamous-cell lung cancer with incidental myocardial metastasis. *J Emerg Med.* 2015;49:e153-4. <http://dx.doi.org/10.1016/j.jemermed.2015.03.015>.
 63. Romano A, Grassia M, Rossetti AR, Esposito G, Braccio B, Pezzella M, et al. Sarcomatoid carcinoma of the lung: a rare case of three small intestinal intussusceptions and literature review. *Int J Surg Case Rep.* 2015;13:48-50. <http://dx.doi.org/10.1016/j.ijscr.2015.05.025>.
 64. Nunes V, Santiago I, Marinho R, Pires D, Theias R, Gomes A, et al. Duodeno-colic fistula as a rare presentation of lung cancer — surgical treatment of a stage IV oligometastatic lung disease. *Int J Surg Case Rep.* 2015;13:125-8. <http://dx.doi.org/10.1016/j.ijscr.2015.06.026>.
 65. Iwamuro M, Uetsuka H, Makiyama K, Yamamoto K. Metastatic tumors in the duodenum: a report of two cases. *J Cancer Res Ther.* 2015;11:648. <http://dx.doi.org/10.4103/0973-1482.137675>.
 66. Nakamura T, Chino O, Tajima T, Tanaka Y, Yokoyama D, Hanashi T, et al. Ileal intussusception due to metastasis from squamous cell carcinoma of the lung resected 12 years previously. *Tokai J Exp Clin Med.* 2015;40:137-40.
 67. Fujii Y, Homma S, Yoshida T, Taketomi A. Jejunal intussusception caused by metastasis of a giant cell carcinoma of the lung. *BMJ Case Rep.* 2016;2016. <http://dx.doi.org/10.1136/bcr-2016-216030>.
 68. Gonzalez-Tallon AI, Vasquez-Guerrero J, Garcia-Mayor MA. Colonic metastases from lung carcinoma: a case report and review of the literature. *Gastroenterol Res.* 2013;6:29-33.
 69. Misra SP, Dwivedi M, Misra V, Dharmani S, Gupta M. Duodenal metastases from squamous cell carcinoma of the lung: endoscopic management of bleeding and biliary and duodenal obstruction. *Indian J Gastroenterol.* 2004;23:185-6.
 70. Garrigós L, Iglesias M, Lloreta J, Jimeno J, Arriola E. Metastatic intestinal perforation secondary to a primary lung tumour. *Cir Esp.* 2010;87:257-9. <http://dx.doi.org/10.1016/j.ciresp.2009.03.019>.
 71. AlSaeed EF, Tunio MA, AlSayari K, AlDandan S, Riaz K. Duodenal metastasis from lung adenocarcinoma: a rare cause of melena. *Int J Surg Case Rep.* 2015;13:91-4. <http://dx.doi.org/10.1016/j.ijscr.2015.06.019>.
 72. Rossi G, Marchioni A, Romagnani E, Bertolini F, Longo L, Cavazza A, et al. Primary lung cancer presenting with gastrointestinal tract involvement: clinicopathologic and immunohistochemical features in a series of 18 consecutive cases. *J Thorac Oncol.* 2007;2:115-20.
 73. Hillenbrand A, Sträter J, Henne-Bruns D. Frequency, symptoms and outcome of intestinal metastases of bronchopulmonary cancer. Case report and review of the literature. *Int Semin Surg Oncol.* 2005;6:13.
 74. Romera-Barba E, Castañer-Ramón-Llín J, Navarro-García I, Carrillo López MJ, Sánchez Pérez A, Vazquez-Rojas JL. Metastatic intestinal obstruction secondary to a primary lung tumour. *Gastroenterol Hepatol.* 2016;39:466-8. <http://dx.doi.org/10.1016/j.gastrohep.2015.06.001>.
 75. Usmanij EA, de Geus-Oei LF, Bussink J, Oyen WJ. Update on F-18-fluoro-deoxy-glucose-PET/computed tomography in nonsmall cell lung cancer. *Curr Opin Pulm Med.* 2015;21:314-21. <http://dx.doi.org/10.1097/MCP.0000000000000182>.
 76. Huang YM, Hsieh TY, Chen JR, Chien HP, Chang PH, Wang CH, et al. Gastric and colonic metastases from primary lung adenocarcinoma: a case report and review of the literature. *Oncol Lett.* 2012;4:517-20.
 77. Linsen PV, Linsen VM, Buunk G, Arnold DE, Aerts JG. Iron deficiency anemia as initial presentation of a non-small cell lung carcinoma: a case report. *Respir Med Case Rep.* 2015;11:109-11. <http://dx.doi.org/10.1016/j.rmcr.2015.09.005>.
 78. Leduc C, Prim N, Mennecier B, Delvaux M, Gangi A, Quoix E. Diagnosis of jejunal metastases from lung cancer using capsule endoscopy. *Case Rep Oncol.* 2016;9:526-9.
 79. McNeill PM, Wagman LD, Neifeld JP. Small bowel metastases from primary carcinoma of the lung. *Cancer.* 1987;59:1486-9.
 80. Vailati C, Dainese E, Parente F. An unusual case of right lower abdominal pain. *Gastroenterology.* 2016;151:e13-4. <http://dx.doi.org/10.1053/j.gastro.2016.04.011>.