



## Original article

# Evaluation of an enhanced recovery after lung surgery (ERALS) program in lung cancer lobectomy: An eight-year experience

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## A B S T R A C T

**Introduction:** Enhanced recovery after lung surgery (ERALS) protocols have proven useful in reducing postoperative stay (POS) and postoperative complications (POC). We studied the performance of an ERALS program for lung cancer lobectomy in our institution, aiming to identify which factors are associated with a reduction of POC and POS.

**Methods:** Analytic retrospective observational study conducted in a tertiary care teaching hospital involving patients submitted to lobectomy for lung cancer and included in an ERALS program. Univariable and multivariable analysis were employed to identify factors associated with increased risk of POC and prolonged POS.

**Results:** A total 624 patients were enrolled in the ERALS program. The median POS was 4 days (range 1–63), with 2.9% of ICU postoperative admission. A videothoracoscopic approach was used in 66.6% of cases, and 174 patients (27.9%) experienced at least one POC. Perioperative mortality rate was 0.8% (5 cases). Mobilization to chair in the first 24 h after surgery was achieved in 82.5% of cases, with 46.5% of patients achieving ambulation in the first 24 h. Absence of mobilization to chair and preoperative FEV1% less than 60% predicted, were identified as independent risk factors for POC, while thoracotomy approach and the presence of POC predicted prolonged POS.

**Conclusions:** We observed a reduction in ICU admissions and POS contemporaneous with the use of an ERALS program in our institution. We demonstrated that early mobilization and videothoracoscopic approach are modifiable independent predictors of reduced POC and POS, respectively.

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## Evaluación de un programa de rehabilitación multimodal en lobectomía por cáncer de pulmón: experiencia de 8 años

### RESUMEN

#### Palabras clave:

Rehabilitación multimodal  
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**Introducción:** Los programas de recuperación intensificada en cirugía de pulmón (por sus siglas en inglés, ERALS) han demostrado ser útiles para reducir la estancia hospitalaria y las complicaciones postoperatorias. Estudiamos los resultados de la aplicación de un programa ERALS para lobectomía por cáncer en nuestro centro con la intención de identificar aquellos factores que se relacionan con la reducción de las complicaciones y la estancia.

**Métodos:** Estudio observacional retrospectivo en pacientes sometidos a lobectomía por cáncer de pulmón e incluidos en un programa ERALS. Se empleó análisis univariable y multivariable para identificar los factores de riesgo de complicaciones y estancia prolongada.

**Resultados:** Un total de 624 pacientes se inscribieron en el programa ERALS. La estancia postoperatoria mediana fue de 4 días (1-63), con una tasa de ingreso en la UCI del 2,9%. El abordaje videotoracoscópico fue empleado en el 66,6% de los casos, y la tasa de complicaciones postoperatorias fue del 27,9%, con una tasa de mortalidad del 0,8% (5 casos). La no movilización en las primeras 24 h, y el FEV1% inferior al 60% del previsto, se identificaron como factores de riesgo de complicaciones; mientras que el abordaje mediante toracotomía y la presencia de complicaciones predijeron la estancia prolongada.

**Conclusiones:** Observamos una reducción en la estancia hospitalaria y en los ingresos postoperatorios en la UCI concomitante a la puesta en marcha de un programa ERALS en nuestro centro. La movilización precoz y el abordaje quirúrgico videotoracoscópico demostraron ser predictores independientes y modificables para la reducción de las complicaciones y para la duración de la estancia, respectivamente.

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## Introduction

Enhanced recovery after lung surgery (ERALS) protocols have shown promising results in terms of improving clinical outcomes in patients submitted to lobectomy for lung cancer.<sup>1-6</sup> Video Assisted Thoracoscopic Surgery (VATS) together with early mobilization were soon identified as independent predictors of shorter postoperative stay (POS)<sup>3,5,7</sup> and reduction of postoperative complications (POC).<sup>3,7,8</sup> These measures, together with early restoring of oral feeding, avoidance of opioids in the postoperative period and chest tube removal politics are considered fundamental components of ERALS programs in recently published guidelines.<sup>9</sup> Despite its possible benefits, the performance of ERALS reportedly varies significantly,<sup>10,11</sup> which is likely attributable in part to variations in individual, organizational, or cultural factors that can hinder comprehensive implementation of these programs.<sup>12,13</sup> The potential influence of these external factors may also make it difficult to identify independent and reliable predictors of outcomes and their variability between healthcare providers.<sup>2,13</sup>

At the end of 2012, we launched an ERALS program in our institution. Patients spent the day of surgery (postoperative day 0 [POD 0]) in the postanesthetic care unit (PACU) under direct supervision of the anesthesia team, commencing postoperative measures of the ERALS protocol on arrival in the PACU (Table 1). In the present work, we study the performance of our ERALS program 8 years after its launch.

The primary objective is to evaluate the results of this ERALS program in terms of clinical outcomes and hospital stay. As a secondary objective, we intend to identify which factors are associated with increased risk for POC and prolonged POS.

## Methods

This analytic retrospective observational study was carried out in a tertiary care teaching hospital. After obtaining authorization from the hospital's ethics committee, we studied data of patients included in an ERALS program in our institution. We included all adult patients ( $\geq 18$  years) who had undergone scheduled lobectomy for suspected or confirmed lung cancer between 1 December 2012 and 31 October 2020. Exclusion criteria were emergency surgery, non-oncological lung resection surgery, and oncological lung surgery involving other chest wall structures. We reviewed the electronic and paper-based medical records (available in digitized format) up to 12 months after discharge from hospital. We recorded patient characteristics, presence of comorbidities, and data on intervention and perioperative care (Table 2). Major postoperative complications were defined according to the modified criteria proposed by previous authors,<sup>14</sup> applying the Clavien-Dindo classification based on the treatment required<sup>15</sup> (Table 3). Perioperative mortality (occurring within 30 days after the operation or later if patient was still an inpatient,<sup>16</sup> reoperation rate during admission and

**Table 1 – Standards of care for oncologic lung resection surgery in our institution. Pre-ERALS versus ERALS periods.**

	Pre-ERALS (absence of specific protocol)	ERALS
<i>Preoperative period</i>		
Recommendation for smoking cessation at least 4 weeks before surgery	AAD/ASD	Systematic advice by surgeon and anesthesiologist Patients referred to specific anti-smoking office
Patient education/counseling in the surgeon's office	+	+
Prehabilitation for patients with borderline lung function or exercise capacity	ASD	+
<i>Perioperative period</i>		
Oral carbohydrate loading two hours before surgery	–	–
Avoidance of routine preoperative sedation	–	–
Preferent use of epidural/paravertebral block	+	+
Venous thromboembolism prophylaxis in major lung resection procedures	Systematic postoperative use of low-molecular-weight-heparin. Mechanical prophylaxis ASD	Like pre-ERALS
Routine use of antibiotic prior to skin incision	+	+
Systematic use of Chlorhexidine–alcohol instead of povidone-iodine solution for skin preparation	–	+
Use of VATS	ASD	+
Muscle-sparing technique if a thoracotomy is required	ASD	+
Systematic prophylaxis of perioperative nausea and vomiting	AAD	+
Perioperative maintenance of normothermia with convective active warming devices	AAD	+
Use of one single chest tube	ASD	+
Lung-protective strategies used during one-lung ventilation	–	AAD
Use of short-acting volatile or intravenous anesthetics	AAD	+
Use of balanced crystalloids	+	+
Systematic extubation in operating room (unless specific conditions)	+	+
<i>Postoperative period</i>		
Incentive spirometer in the first two hours after surgery	–	+
Preferential use of acetaminophen and NSAIDs regularly administered unless contraindications exist	AAD	+
Systematic use of dexamethasone to prevent PONV and reduce pain	–	AAD
Continuation of preoperative beta-blockers during the postoperative period	AAD/ASD	+
Mobilization to chair	On POD 1	On POD 0 (4–6 h after arrival in the PACU)
Postoperative chest X-ray	In the first 24 h	2–4 h after arrival in the PACU
Arterial catheter withdrawal	AAD	On the first 4–6 h after arrival in the PACU
Oral intake	ASD	4 h after arrival in the PACU Clear liquids by evening-night
Urinary catheter withdrawal in the morning of POD1	–	+
Physiotherapist instructed non-complex training exercise and promoted ambulation in the morning of POD 1	+	+
CD: avoidance of routine application of external suction	+	+
Use of digital drainage systems always when available	–	+
CD removal even if the daily serous effusion is of high volume (up to 450 ml/24 h)	ASD	+
+: systematically applied; –: non applied; AAD: at the anesthesiologist's discretion; ASD: at the surgeon's discretion; CD: chest drain; ERALS: enhanced recovery after lung surgery; NSAIDs: non-steroidal anti-inflammatory drugs; PACU: postanesthetic care unit; POD: postoperative day. PONV: postoperative nausea and vomiting; VATS: video assisted thoracoscopic surgery.		

hospital readmissions within 30 days of discharge were also recorded (Table 2). A prolonged POS was defined as  $\geq$  the 75th percentile<sup>17,18</sup> ( $\geq$  six days). Prolonged air leak was defined as persisting for more than 5 days after the intervention.<sup>19,20</sup> Data

collection was carried out between 1 March and 30 November 2020. Patients' data were anonymized. We have reported this study in accordance with the STROBE criteria for observational studies.

**Table 2 – Distribution of individual's characteristics, perioperative data, and outcomes of patients submitted to lung cancer lobectomy under an ERALS program.**

	n = 624
<b>Individual characteristics</b>	
Age (years)	64.8 ± 11
Male sex	474 (75.8)
Weight (kg)	76.9 ± 15
BMI	27.5 ± 5
History of smoking	500 (83.8)
Pack-year	52 [0–175]
Hypertension	315 (50.6)
Diabetes mellitus	141 (22.6)
Ischemic heart disease	59 (9.5)
Atrial fibrillation	36 (5.8)
COPD	208 (34.8)
COPD ≥ 3 grade GOLD	21 (3.4)
OSAS	44 (7.1)
ASA grade ≥ 3	354 (56.8)
FVC %	97.2 ± 17
FEV1%	84.8 ± 20
Individuals with FEV1% <sub>predicted</sub> < 60% <sup>d</sup>	68 (10.9)
Individuals with DLCO % <sub>predicted</sub> < 60% <sup>d</sup>	104 (16.7)
<b>Perioperative factors and outcomes</b>	
VATS approach	399 (66.6)
Analgesia via epidural/paravertebral/intercostal catheters	558 (90.6)
Infusion of vasopressors during the intervention	33 (5.3)
Reoperation during admission	15 (2.4)
Admission to the ICU	18 (2.9)
Readmission to the ICU	21 (3.4)
POS	4 [1–63]
Prolonged POS	185 (29.9)
Mortality at 30 days/during admission	5 (0.8)
POC <sup>a</sup>	174 (27.9)
Respiratory POC <sup>b</sup>	161 (25.8)
Cardiovascular POC <sup>c</sup>	27 (4.3)
Individual POC	259 (41.5)
Subcutaneous/mediastinal emphysema	83 (13.4)
Atelectasis	23 (3.7)
Pneumonia	8 (1.3)
Suspected pneumonia	1
Empyema	2
Bronchospasm	5
Hemo/pneumothorax	14 (2.2)
Bronchopleural fistula	2
Reintubation requirement	7 (1.1)
Chest wall hematoma	1
Acute respiratory distress syndrome ≥ moderate	4
Hypoxemia requiring therapy	9 (1.4)
New-onset atrial fibrillation	17 (2.7)
Myocardial infarction/injury	1
Other cardiovascular complications (congestive cardiac failure, major cardiac arrhythmia other than atrial fibrillation)	9 (1.4)
Prolonged air leak <sup>d</sup>	64 (10.3)
Postoperative ileus	1
Fever of unknown origin	2
Other <sup>e</sup>	6 (1)
Days of permanence of the CD (excluded cases with prolonged air leak) <sup>d</sup>	3 (1–15)
Hospital discharge with CD	43 (6.9)
Oral intake on POD 0 <sup>d</sup>	401 (64.4)
Incentive spirometer on POD 0	573 (94.9)
Mobilization to chair in the first 24 h after surgery <sup>d</sup>	514 (82.5)
Ambulation in the first 24 h after surgery <sup>d</sup>	290 (46.5)

**Table 2 (Continued)**

	n = 624
Arterial withdrawal on POD 0	237 (37.9)
Intravenous fluid therapy withdrawal in the first 24 h after surgery	512 (85.3)
Urinary catheter withdrawal in the first 24 h after surgery	498 (83)
30-Day readmission <sup>f</sup>	22 (3.5)
Emphysema/Pneumothorax	4
Dyspnea	4
Pneumonia/pleural empyema	5
Bronchopleural fistula	2
Other	7 (1.1)

ASA: American Society of Anesthesiologists; BMI: body mass index; COPD: chronic obstructive pulmonary disease; CD: chest drain; DLCO%: diffusing capacity of the lungs for carbon monoxide percentage of predicted; ERALS: enhanced recovery after lung surgery; FEV1% forced expiratory volume in the first second percentage of predicted; FVC: forced vital capacity percentage of predicted; GOLD: Global Initiative for Obstructive Lung Disease; ICU: Intensive Care Unit; OSAS: obstructive sleep apnea syndrome; POC: postoperative complications; POD: postoperative day; POS: postoperative stay; VATS: video assisted thoracoscopic surgery. Data are listed as n (percentage) for categorical variables and mean ± standard deviation or median [interquartile range] for continuous variables. Missing values have been excluded for the estimation of percentages.

<sup>a</sup> Composite variable (considered positive if any respiratory, cardiovascular, or intervention-related complication was present).

<sup>b</sup> Composite variable (considered positive if at least one respiratory complication was present).

<sup>c</sup> Composite variable (considered positive if at least one cardiovascular complication was present).

<sup>d</sup> Missing values replaced using multiple imputation (Regression Method).

<sup>e</sup> See Table 3.

<sup>f</sup> Either in our center or at patient's hospital of origin.

### Perioperative management in lung resection surgery

Specific perioperative management of ERALS patients is detailed in Table 1. VATS approach is systematically used except in patients in whom a pneumonectomy, superior sulcus tumor, or tumors that invade the chest wall are prevented. Patients spent the first postoperative night in the PACU. Incentive spirometry instructed by the nurse was promoted in the first two hours after arrival at the PACU, with the beginning of oral tolerance to clear liquids 4 h after admission and mobilization to the chair on the evening of POD 0 if the patient's conditions allowed it. Patients were transferred to the ward on the morning of POD 1 unless specific conditions delayed transfer. Any urinary catheter or intravenous fluid therapy was removed on arrival in the ward, and patients were encouraged to immediately sit in a chair. On the morning of POD 1, a physiotherapist worked on the patients, instructing them in a non-complex training exercise and promoting ambulation. Intravenous or oral opioids were avoided and used only for breakthrough pain not controlled by non-steroidal analgesics and/or regional techniques. Epidural or paravertebral catheters were usually kept in situ for the first 48 h after surgery and were not considered an impediment to ambulation. Regional analgesia was usually maintained by

**Table 3 – Postoperative complications based on the treatment required (Clavien-Dindo classification<sup>15</sup>).**

Grade	Complication	n (%) <sup>a</sup>	% <sup>b</sup>
Grado I Any complication without need for pharmacologic treatment or other intervention	–	–	–
Grade II Complication that requires pharmacologic treatment or minor intervention only	Chest wall hematoma	1	
	Subcutaneous/mediastinal emphysema	82 (13.1)	47.1
	Prolonged air leak	64 (10.2)	36.8
	Atelectasis	23 (3.7)	13.2
	Bronchospasm	4 (0.6)	2.3
	Hypoxemia requiring oxygen therapy	8 (1.3)	4.6
	Pneumonia	2 (0.3)	1.1
	Suspected pneumonia	1	0.5
	Pleural empyema	2	1.1
	New onset atrial fibrillation	14	8
	Myocardial infarction/injury	1	0.5
	Other cardiovascular complications (congestive cardiac failure, major arrhythmia other than atrial fibrillation)	9 (1.4)	5.2
	Postoperative ileus	1	0.5
	Fever of unknown origin	2	1.1
IIIa Complication that requires intervention without general anesthesia	Hemo/pneumothorax	10 (1.6)	5.7
	Upper gastrointestinal bleeding	1	0.5
IIIb Intervention requires general anesthesia	Subcutaneous/mediastinal emphysema	1	0.5
	Bronchopleural fistula	1	0.5
IVa Single organ dysfunction requiring intensive care unit management and life support	New onset atrial fibrillation	3	1.7
	Bronchospasm	1	0.5
	Hypoxemia requiring oxygen therapy	1	0.5
	Hemo/pneumothorax	4 (0.6)	2.3
	Pneumonia	6 (1)	3.4
	Acute respiratory distress syndrome $\geq$ moderate	4 (0.6)	2.3
	Reintubation	7 (1.1)	4
IVb Multiorgan dysfunction requiring intensive care unit management and life support	Sepsis	1	0.5
Grade V Any complication leading to the death of the patient.	Broncho-pleural fistula	1	0.5
	Intestinal volvulus	1	0.5
	Usual interstitial pneumonia	1	0.5
	Surgical bleeding	1	0.5
	Major peripheral ischemic event	1	0.5

<sup>a</sup> Percentage of total sample.

<sup>b</sup> Percentage in the subgroup of patients with complications (n = 174).

infusion of ropivacaine 1–1.5 mg/ml and fentanyl 1–2  $\mu$ g/ml in saline, the infusion rates being 5–7 and 7–12 ml/h for epidural and paravertebral/intercostal catheters, respectively. Digital chest drain was systematically used (*Thopaz Chest Drain System*<sup>®</sup>, Medela, Spain) and removed on POD 2 in the absence of air leak and if serous output was less than 450 ml/24 h. Patients with prolonged air leak were discharged with portable chest drain at the surgeon's discretion.

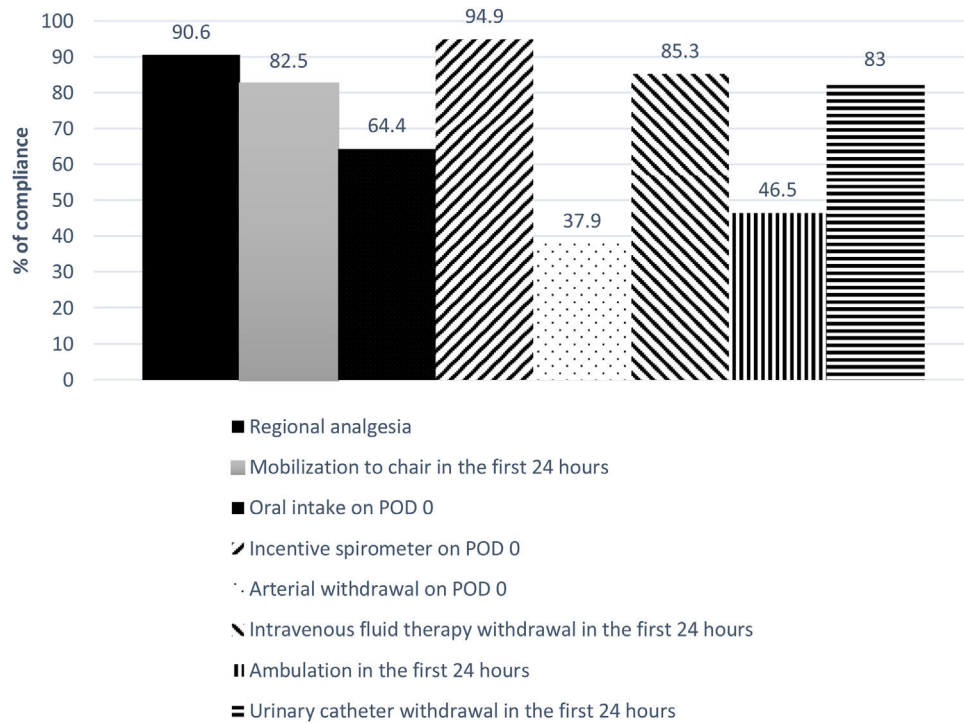
### Statistical analysis

Statistical analysis was performed by the primary researcher using SPSS version 22.0. © for Windows (SPSS Inc., Chicago, USA). Continuous variables are presented as the mean, standard deviation and median with range (minimum and maximum values), and categorical variables as absolute and marginal frequencies and proportions. For those variables with missing data > 5%, the replacement of missing values by multiple imputation (Regression Method) was used. The proportions for categorical variables with less than 5% missing

values were estimated from the original available data. Normality of continuous variables was examined using the Kolmogorov–Smirnov test and the homogeneity of variances with the Levene test. We used Student's t-test or Mann–Whitney U test and  $\chi^2$  test (or Fisher's test) to assess the behavior of the means and proportions of continuous and categorical variables, respectively. Variables associated with increased risk of POC and prolonged POS were analyzed by multivariable analysis (binary logistic regression).

### Results

A total of 624 patients were enrolled in the ERALS program. **Table 2** shows the distribution of patient characteristics and perioperative data, together with outcomes. A VATS approach was used in 66.6% of the cases, with a prominent use of regional analgesia via an epidural, paravertebral, or intercostal catheter (90.6%). Admission to the ICU was anecdotal (2.9%). The median POS was 4 days (interquartile range 3–6 days). A



**Fig. 1 – Compliance with the postoperative components of the ERALS protocol.**

total of 259 individual complications were experienced by 174 patients (27.9%) (Tables 2 and 3). The overall perioperative mortality rate was 0.8% (5 cases). The main cause of in-hospital mortality was respiratory failure (one case due to persistent bronchopleural fistula, another case in a patient reoperated for intestinal volvulus, and a patient with acute exacerbation of pre-existing usual interstitial pneumonia). One patient died during the intervention due to uncontrollable bleeding, and one due to major peripheral ischemic event in the postoperative period. Univariable analysis of mortality showed no risk factors association.

The global compliance with the different components of the ERALS program is shown in Fig. 1. Mobilization to chair in the first 24 h after surgery was achieved in 82.5% of cases. Of these, a total 46.5% of patients achieved ambulation in the first 24 h. Absence of mobilization to chair in the first 24 h after surgery together with preoperative FEV1% less than 60% predicted were identified as independent risk factors for POC (Table 4), while non-VATS approach and the presence of POC predicted prolonged POS (Table 5).

A total 10.3% of the cases experienced air leak lasting more than 5 days. The median duration of permanence of the chest drainage (excluded cases with prolonged air leak) was 3 days (Table 2). A total of 43 patients (6.9%) were discharged with outpatient chest drainage due to prolonged air leak (42) or persistent pleural effusion (1).

## Discussion

As far as we know, this is the largest study of these characteristics published in our country.<sup>21</sup> We observed 30-

day mortality and POC rates consistent with recently reported data on ERALS lobectomy.<sup>2,4,22,23</sup> Contradictory data have been reported regarding mortality depending on the population under study, the surgical approach, and the experience of the surgical teams, with figures ranging from zero<sup>3,4,7,24</sup> to more than 3%.<sup>2</sup> Different authors argue that 90-day mortality would better address procedure-related deaths than 30-day mortality, as some patients die beyond the first 30 days after surgery.<sup>25–27</sup> In this sense, we could be underestimating the mortality attributable to the operation in our sample, even though we reported mortality figures beyond POD 30 if patient was still an inpatient. The POS in our sample was similar to, or slightly higher than, those recently published for ERALS programs, the median reported POS for lobectomies ranging from 4–5<sup>2,5,7,22,28</sup> to 1–2 days.<sup>3,24,28,29</sup> Our published data on a historical cohort of patients who underwent lobectomy and were treated conventionally in the two years prior to the start of the program: pre-ERALS cohort (1 January 2010–30 November 2012)<sup>30</sup> showed a median hospital stay of 7 days (interquartile range 6–8 days) and 41.6% of postoperative ICU admissions, this reflecting a clear change in trend following the launch of the ERALS program.

We demonstrated how mobilization to chair in the first 24 h following intervention has a beneficial effect in terms of reducing POC, while VATS approach allowed a reduction in POS. These two modifiable factors have been previously addressed as independent predictors of outcomes.<sup>3,5,7,8</sup> Other authors have reported that implementation of intensive early mobilization can drastically reduce the POS.<sup>3,24,29</sup> Das Neves Pereira et al. reported that more than 90% of patients who participated in an aggressive ERALS program and underwent lobectomy for lung cancer achieved ambulation in the first

**Table 4 – Variables associated with the incidence of postoperative complications.**

Variables	Univariable		Multivariable	
	OR (CI 95%)	p-Value	OR (CI 95%)	p-Value
Male sex	1.9 (1.2–3)	0.03	1.4 (0.8–2.6)	0.218
Age		0.01		0.093
Age ( $\geq 65$ years)	1.6 (1.1–2.3)	0.02	1.6 (1–2.7)	0.341
VATS	1.1 (0.8–1.7)	0.326		
FEV1%		<0.001		0.593
FEV1% < 60%	<b>3 (1.7–5.2)</b>	<b>&lt;0.001</b>	<b>2.1 (1–4)</b>	<b>0.04</b>
DLC0% < 60%	2.5 (1.5–3.9)	<0.001	1.8 (0.9–3.2)	0.092
COPD GOLD $\geq 3$	5.1 (2–13)	<0.001	1.9 (0.5–8.2)	0.561
ASA grade $\geq 3$	1.8 (1.2–2.6)	0.002	1 (0.6–1.6)	0.274
Ambulation in the first 24 h after surgery	0.5 (0.4–0.7)	0.041	0.8 (0.5–1.3)	0.096
Mobilization to chair in the first 24 h after surgery	<b>0.3 (0.17–0.4)</b>	<b>&lt;0.001</b>	<b>0.34 (0.2–0.7)</b>	<b>0.002</b>
Oral intake on POD 0	0.6 (0.4–0.9)	0.01	1.1 (0.7–1.8)	0.721

ASA: American Society of Anesthesiologists classification; BMI: body mass index; COPD: chronic obstructive pulmonary disease; DLC0%: diffusing capacity of the lungs for carbon monoxide, percentage of predicted; FEV1%: forced expiratory volume in the first second, percentage of predicted; GOLD: Global Initiative for Obstructive Lung Disease; POD: postoperative day; VATS: video assisted thoracoscopic surgery.

**Table 5 – Variables associated with prolonged postoperative stay.**

Variables	Univariable		Multivariable	
	OR (CI 95%)	p-Value	OR (CI 95%)	p-Value
Male sex	1.5 (1–2.3)	0.04	1.8 (1–3.4)	0.614
Age ( $\geq 65$ years)	1.3 (0.9–1.8)	0.273	–	–
VATS	<b>0.3 (0.2–0.5)</b>	<b>&lt;0.001</b>	<b>0.31 (0.2–0.5)</b>	<b>&lt;0.001</b>
FEV1% < 60%	1.6 (1–2.7)	0.05	1 (0.4–2.5)	0.417
DLC0% < 60%	1.6 (1–2.5)	0.03	1.6 (0.8–3.3)	0.142
COPD	1.9 (1.4–2.8)	<0.001	0.9 (0.5–1.6)	0.871
COPD GOLD $\geq 3$	1.5 (0.6–3.8)	0.342	–	–
ASA grade $\geq 3$	1.6 (1.1–2.3)	0.01	1 (0.6–1.6)	0.312
Ambulation in the first 24 h after surgery	0.6 (0.4–0.9)	0.009	1 (0.5–2.1)	0.146
Mobilization to chair in the first 24 h after surgery	0.4 (0.3–0.7)	<0.001	0.8 (0.4–1.7)	0.621
Oral intake on POD 0	0.7 (0.5–1)	0.05	1 (0.9–2.4)	0.921
POC	<b>4.2 (2.8–6)</b>	<b>&lt;0.001</b>	<b>4.1 (2.5–6.7)</b>	<b>&lt;0.001</b>

ASA: American Society of Anesthesiologists classification; BMI: body mass index; COPD: chronic obstructive pulmonary disease; DLC0%: diffusing capacity of the lungs for carbon monoxide, percentage of predicted; FEV1%: forced expiratory volume in the first second, percentage of predicted; GOLD: Global Initiative for Obstructive Lung Disease classification; POC: postoperative complication; POD: postoperative day; VATS: video assisted thoracoscopic surgery.

postoperative hour, demonstrating an independent correlation between early ambulation and reduced POC.<sup>3</sup> More recently, Mayor et al. reported a median POS of 1 day after VATS lobectomy in patients subjected to a specific early mobilization protocol.<sup>29</sup> Although our results in terms of ambulation in the first 24 h after surgery (46.5%) agree with some of those previously reported,<sup>4</sup> they are still far from the best published rates, which are greater than 80% of patients achieving mobilization to chair or ambulation on POD 0.<sup>3,7,24,29</sup>

Some of the factors that may have influenced our improvable results are that we do not have a step-down unit for ERALS patients in our center and no nursing staff in the PACU are specifically dedicated to the care of these patients. Additionally, although the ERALS protocol is well established in the unit, the high turnover of patients, high levels of demand for care, and frequent replacement of personnel hinder homogeneous and effective application of the protocol on POD 0. Inadequate staffing and lack of financial resources have been identified as barriers to the optimal implementation of ERAS programs.<sup>12</sup> Although we did not specifically analyze

this aspect, the ratio of nurses to patients in the PACU (going from 1:4 to 1:6), together with the concomitant increase in demands for care caused by the launch of other ERAS programs, probably impacted our results. We must point out that the reduction in ICU admissions observed in the ERALS period could be explained due to institutional protocol changes congruent with the ERALS program rather than due to a difference in the clinical status of the patients. In the pre-ERALS period, patients were referred to ICU in the presence of moderate to severe impaired cardiopulmonary or renal function [examples include (but not limited to): history of ischaemic heart disease or heart failure, stroke or transient ischaemic attack, poorly controlled diabetes mellitus, chronic obstructive pulmonary disease  $\geq 3$  grade GOLD (Global Initiative for Obstructive Lung Disease) and end stage renal disease undergoing dialysis], or any other clinical or intervention-related condition at the discretion of the anesthesiologist.

Whether the “natural” evolution of standards of care contemporary with introduction of ERALS programs, such as the use of VATS and promotion of early mobilization, alone

explains the improvement in outcomes remains a matter of debate.<sup>2,13,31,32</sup> Several authors have reported that greater compliance with ERALS programs is associated with better results, indicating that the different variables involved in these pathways potentially have a summative effect.<sup>5,7</sup> However, although global compliance with ERALS protocols has been identified as having influenced outcomes, only some specific aspects of these protocols have been shown to be independent predictors of outcomes.<sup>3,5,7</sup> Forster et al. reported that early removal of chest tubes, use of electronic drainage systems, cessation of opioids on POD 3, and early feeding are independently associated with a reduction in rate of complications.<sup>7</sup> As these authors have pointed out, which variables are included in multivariable analysis “can lead to a misinterpretation of the results”; for example, does either an early withdrawal of chest drainage or discontinuation of opioids reflect a protective effect on POC, or do they simply reflect that the patient is in better condition? Rogers et al. have shown that global compliance predicts POC but not POS, the latter showing independent correlations with early mobilization, preoperative carbohydrate-rich drinks, and implementation of VATS.<sup>5</sup> We are therefore uncertain whether we should direct our efforts to improving outcomes by implementing a global strategy based on the summative effect of marginal gains, each with its specific cost, or focus on enhancing aspects that have been identified as independent predictors of outcomes. Our uncertainty is compounded by the fact that some of the main factors influencing POS, such as management of air leaks, are not exclusively ERALS but also depend on culture and organization.<sup>13,29,33</sup> As pointed out by other authors, “management of chest tubes remains a critical aspect in the postoperative course of patients following lung resection”.<sup>20</sup> We observed a non-negligible number of drains not removed after ceasing the air leak, this reflecting the everyday practice versus the established ERALS criteria, and moreover probably influencing our improvable POS. Whether a more aggressive withdrawal policy following the published recommendations<sup>9</sup> would have had an impact on our results is something that should be addressed in coming works.

The main shortcoming of our study is its retrospective nature and the potential risk of having underestimated the incidence of the selected factors. Our data were drawn from a single center with specific conditions; thus, our results are not necessarily applicable to other healthcare providers. Another shortcoming of our work was the exclusion of preoperative components of the ERALS program from the analysis. Indeed, some relevant aspects of the ERALS programs, as preoperative carbohydrate-rich drinks, had not yet been incorporated into our protocol and therefore not analyzed. This latter reflecting the heterogeneity previously described when implementing ERALS pathways.<sup>6,10</sup>

As other authors point out, the inclusion of patients undergoing surgery over a period where minimally invasive techniques were being used to varying degrees may introduce substantial bias, as the increased use of VATS or the cultural transformation towards a more proactive attitude may have influenced the results.<sup>32</sup> In this sense, it is likely that over the 8 years included in the analysis the management of these patients regardless of ERALS protocols has been streamlined.

Despite these limitations, we demonstrated the feasibility of incorporating an ERALS protocol in our institution, with statistics of POS and ICU admissions that improve our historical figures. We have shown that, even in the presence of various limitations to implementing an ERALS protocol in a Spanish public center, the results obtained support this practice.

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## Conclusions

We observed a reduction in ICU admissions and POS contemporaneous with the use of an ERALS program in our institution. We demonstrated that mobilization in the first 24 h after surgery and VATS approach are modifiable independent predictors for the reduction of POC and POS, respectively. New prospective and well-designed studies are needed to address the impacts of the overall performance of an ERALS program versus the impacts of improvement in specific elements of special relevance, to identify the crucial factors.

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## Conflict of interest

The authors declare that they have no conflict of interest.

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## REFERENCES

- Madani A, Fiore JF Jr, Wang Y, Bejjani J, Sivikumaran L, Mata J, et al. An enhanced recovery pathway reduces duration of stay and complications after open pulmonary lobectomy. *Surgery*. 2015;158:899–908. <http://dx.doi.org/10.1016/j.surg.2015.04.046>.
- Brunelli A, Thomas C, Dinesh P, Lumb A. Enhanced recovery pathway versus standard care in patients undergoing video-assisted thoracoscopic lobectomy. *J Thorac Cardiovasc Surg*. 2017;154:2084–90. <http://dx.doi.org/10.1016/j.jtcvs.2017.06.037>.
- Das-Neves-Pereira JC, Bagan P, Coimbra-Israel AP, Grimaillof-Junior A, César-López G, Miláñez-de-Campos JR, et al. Fast-track rehabilitation for lung cancer lobectomy: a five-year experience. *Eur J Cardiothorac Surg*. 2009;36:383–92. <http://dx.doi.org/10.1016/j.ejcts.2009.02.020>.
- Haro GJ, Sheu B, Marcus SG, Sarin A, Campbell L, Jablons DM, et al. Perioperative lung resection outcomes after implementation of a multidisciplinary. Evidence-based



- thoracic ERAS program. *Ann Surg*. 2019. <http://dx.doi.org/10.1097/sla.0000000000003719>. Epub ahead of print. PMID: 31851005.
5. Rogers LJ, Bleetman D, Messenger DE, Joshi NA, Wood L, Rasburn NJ, et al. The impact of enhanced recovery after surgery (ERAS) protocol compliance on morbidity from resection for primary lung cancer. *J Thorac Cardiovasc Surg*. 2018;155:1843–52. <http://dx.doi.org/10.1016/j.jtcvs.2017.10.151>.
  6. Van Haren RM, Atay SM. Enhancing the study of enhanced recovery after thoracic surgery: methodology and population-based approaches for the future. *J Thorac Dis*. 2019;11:S612–8. <http://dx.doi.org/10.21037/jtd.2019.01.81>.
  7. Forster C, Doucet V, Perentes JY, Abdelnour-Berchtold E, Zellweger M, Marcucci C, et al. Impact of compliance with components of an ERAS pathway on the outcomes of anatomic VATS pulmonary resections. *J Cardiothorac Vasc Anesth*. 2020;34:1858–66. <http://dx.doi.org/10.1053/j.jvca.2020.01.038>.
  8. Muehling BM, Halter GL, Schelzig H, Meierhenrich R, Steffen P, Sunder-Plassmann L, et al. Reduction of postoperative pulmonary complications after lung surgery using a fast track clinical pathway. *Eur J Cardiothorac Surg*. 2008;34:174–80. <http://dx.doi.org/10.1016/j.ejcts.2008.04.009>.
  9. Batchelor TJP, Rasburn NJ, Abdelnour-Berchtold E, Brunelli A, Cerfolio RJ, González M, et al. Guidelines for enhanced recovery after lung surgery: Recommendations of the Enhanced Recovery after Surgery (ERAS®) Society and the European Society of Thoracic Surgeons (ESTS). *Eur J Cardiothorac Surg*. 2019;55:91–115. <http://dx.doi.org/10.1093/ejcts/ezy301>.
  10. von Meyenfeldt EM, de Betue CTI, van den Berg R, van Thiel ERE, Schreurs WH, Marres GMH. Wide variation in perioperative care in anatomical lung resections in the Netherlands: a national survey. *Semin Thorac Cardiovasc Surg*. 2020;32:1101–10. <http://dx.doi.org/10.1053/j.semtcvs.2020.05.015>.
  11. Medbery RL, Fernandez FG, Khullar OV. ERAS and patient reported outcomes in thoracic surgery: a review of current data. *J Thorac Dis*. 2019;11 Suppl. 7:S976–86. <http://dx.doi.org/10.21037/jtd.2019.04.08>.
  12. Pearsall EA, Meghji Z, Pitzul KB, Aarts MAe, McKenzie M, McLeod RS, et al. A qualitative study to understand the barriers and enablers in implementing an enhanced recovery after surgery program. *Ann Surg*. 2015;261:92–6. <http://dx.doi.org/10.1097/SLA.0000000000000604>.
  13. Bertolaccini L, Rocco G, Crisci R, Solli P. Enhanced recovery after surgery protocols in video-assisted thoracic surgery lobectomies: the best is yet still to come? *J Thorac Dis*. 2018;10:S493–6. <http://dx.doi.org/10.21037/jtd.2018.02.33>.
  14. Jammer I, Wickboldt N, Sander M, Smith A, Schultz MJ, Pelosi P, et al. Standards for definitions and use of outcome measures for clinical effectiveness research in perioperative medicine: European Perioperative Clinical Outcome (EPCO) definitions: a statement from the ESA-ESICM joint taskforce on perioperative outcome measures. *Eur J Anaesthesiol*. 2015;32:88–105. <http://dx.doi.org/10.1097/EJA.0000000000000118>.
  15. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg*. 2004;240:205–13. <http://dx.doi.org/10.1097/01.sla.0000133083.54934.ae>.
  16. Thomas PA, Berbis J, Baste JM, Le Pimpec-Barthes F, Tronc F, Falcoz PE, et al. Pneumonectomy for lung cancer: contemporary national early morbidity and mortality outcomes. *J Thorac Cardiovasc Surg*. 2015;149:73–83. <http://dx.doi.org/10.1016/j.jtcvs.2014.09.063>.
  17. Morimoto Y, Mizuno H, Akamaru Y, Yasumasa K, Noro H, Kono E, et al. Predicting prolonged hospital stay after laparoscopic cholecystectomy. *Asian J Endosc Surg*. 2015;8:289–95. <http://dx.doi.org/10.1111/ases.12183>.
  18. McDevitt J, Kelly M, Comber H, Kelleher T, Dwane F, Sharp L. A population-based study of hospital length of stay and emergency readmission following surgery for non-small-cell lung cancer. *Eur J Cardiothorac Surg*. 2013;44:e253–9. <http://dx.doi.org/10.1093/ejcts/ezt389>.
  19. Mueller MR, Marzluf BA. The anticipation and management of air leaks and residual spaces post lung resection. *J Thorac Dis*. 2014;6:271–84. <http://dx.doi.org/10.3978/j.issn.2072-1439.2013.11.29>.
  20. Pompili C, Miserocchi G. Air leak after lung resection: pathophysiology and patients' implications. *J Thorac Dis*. 2016;8 Suppl. 1:S46–54. <http://dx.doi.org/10.3978/j.issn.2072-1439.2015.11.08>.
  21. Padilla-Alarcón J, Peñalver-Cuesta JC. Experiencia de un programa de fast-track surgery en resección pulmonar. *Arch Bronconeumol*. 2013;49:89–93. <http://dx.doi.org/10.1016/j.arbres.2012.09.011>.
  22. Hubert J, Bourdages-Pageau E, Garneau CAP, Labbé C, Ugalde PA. Enhanced recovery pathways in thoracic surgery: the Quebec experience. *J Thorac Dis*. 2018;10 Suppl. 4:S583–90. <http://dx.doi.org/10.21037/jtd.2018.01.156>.
  23. Van Haren RM, Mehran RJ, Mena GE, Correa AM, Antonoff MB, Baker CM, et al. Enhanced recovery decreases pulmonary and cardiac complications after thoracotomy for lung cancer. *Ann Thorac Surg*. 2018;106:272–9. <http://dx.doi.org/10.1016/j.athoracsur.2018.01.088>.
  24. Khandhar SJ, Schatz CL, Collins DT, Graling PR, Rosner CM, Mahajan AK, et al. Thoracic enhanced recovery with ambulation after surgery: a 6-year experience. *Eur J Cardiothorac Surg*. 2018;53:1192–8. <http://dx.doi.org/10.1093/ejcts/ezy061>.
  25. Millan RR, Berger A, Sima CS, Lou F, Dycoco J, Rusch VW, et al. Thirty-day mortality underestimates the risk of early death after major resections for thoracic malignancies. *Ann Thorac Surg*. 2014;98:1769–74. <http://dx.doi.org/10.1016/j.athoracsur.2014.06.024>.
  26. Pezzi CM, Mallin K, Mendez AS, Gay EG, Putnam JB. Ninety-day mortality after resection for lung cancer is nearly double 30-day mortality. *J Thorac Cardiovasc Surg*. 2014;148:2269–78. <http://dx.doi.org/10.1016/j.jtcvs.2014.07.077>.
  27. Bryant AS, Rudemiller K, Cerfolio RJ. The 30- versus 90-day operative mortality after pulmonary resection. *Ann Thorac Surg*. 2010;89:1717–22. <http://dx.doi.org/10.1016/j.athoracsur.2010.01.069>.
  28. Martin LW, Sarosiek BM, Harrison MA, Hedrick T, Isbell JM, Krupnick AS, et al. Implementing a thoracic enhanced recovery program: lessons learned in the first year. *Ann Thorac Surg*. 2018;105:1597–604. <http://dx.doi.org/10.1016/j.athoracsur.2018.01.080>.
  29. Mayor MA, Khandhar SJ, Chandy J, Fernando HC. Implementing a thoracic enhanced recovery with ambulation after surgery program: key aspects and challenges. *J Thorac Dis*. 2018;10 Suppl. 32:S3809–14. <http://dx.doi.org/10.21037/jtd.2018.10.106>.
  30. De la Matta M, Proyecto ERAS: Una Nueva Fórmula de Gestión Por Procesos. In: Santiago-Martín J, Neira-Reina F, Ortega-García JL, Echevarría-Moreno M, editors. *Actualizaciones de Anestesiología, Reanimación y Tratamiento del Dolor 2016 Sevilla* Ed Liberlibro.com; 2016; p. 377–90. <https://www.file:///C:/Users/User/AppData/Local/Temp/aaearalmeria2016.PDF>
  31. Fiore JF, Bejjani J, Conrad K, Niculiseanu P, Landry T, Lee L, et al. Systematic review of the influence of enhanced recovery pathways in elective lung resection. *J Thorac*

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- Cardiovasc Surg. 2016;151:708-15. <http://dx.doi.org/10.1016/j.jtcvs.2015.09.112>. e6..
32. Detterbeck F, Molins L. Video-assisted thoracic surgery and open chest surgery in lung cancer treatment: present and future. J Vis Surg. 2016;2:173. <http://dx.doi.org/10.21037/jovs.2016.11.03>. eCollection 2016.
33. French DG, Plourde M, Henteleff H, Mujoomdar A, Bethune D. Optimal management of postoperative parenchymal air leaks. J Thorac Dis. 2018;10:S3789-98. <http://dx.doi.org/10.21037/jtd.2018.10.05>.