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Uniportal video-assisted thoracoscopic lobectomy versus other video-assisted thoracoscopic lobectomy techniques: a randomized study

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Abstract

OBJECTIVES: A prospective, randomized study was carried out on patients undergoing lung cancer surgery, with the aim of determining if uniportal video-assisted lobectomy has more favourable postoperative outcomes than other video-assisted thoracoscopic lobectomy techniques (Duke approach and Copenhagen approach).

METHODS: Patients were randomly assigned to two groups; uniportal video-assisted lobectomy (Group A; $n = 51$) and other video-assisted thoracoscopic lobectomy techniques (Group B; $n = 55$). The primary outcome measures were: postoperative pain (analogue visual scale) and supplementary doses of analgesics (morphine, milligrams); the secondary outcome measures were: the delay in removing the paravertebral catheter and the chest drain, the duration of the postoperative hospital stay, postoperative complications and the operative or 30-day mortality. We assessed postoperative pain during the first 3 days to identify possible differences coinciding with paravertebral catheter removal and with the start of mobilization, and we evaluated the type of resection, R0/R1 (a very important factor in assessing postoperative pain). All continuous data were evaluated for normality, and analysed with the Mann–Whitney *U*-tests or *t*-tests. Categorical data were analysed by Fisher's exact test.

RESULTS: One hundred and six lobectomies were completed. Both groups were comparable with respect to different clinical parameters (age, clinical stage and comorbidity), preoperative and pathological variables. The median visual analogue pain score in the first 3 days did not show statistically significant differences (respectively, $P = 0.58$, $P = 0.64$, $P = 0.85$). Likewise, the median morphine use in the first 3 days did not show statistically significant differences (respectively, $P = 0.72$, $P = 0.81$, $P = 0.64$). There was no difference in timing to remove the paravertebral catheter ($P = 0.82$) and the chest drain ($P = 0.65$) and the duration of the postoperative hospital stay ($P = 0.62$). There was no difference in postoperative complications (one reoperation for bleeding in Group B, $P = 0.24$). There was no operative or 30-day mortality in either group.

CONCLUSIONS: Uniportal video-assisted thoracoscopic lobectomy does not present better postoperative outcomes than other video-assisted thoracoscopic lobectomy techniques.

Keywords: Lung cancer surgery • Surgery/incision/exposure/techniques • Thoracoscopy/VATS • Surgery • Complication • Pain

THORACIC

INTRODUCTION

Video-assisted thoracoscopic surgery (VATS) lobectomy is now well established and performed all around the world. Different techniques have been described: uniportal access for VATS was first described in 2004 by Rocco *et al.* [1], and this strategy has been used for numerous indications, including lobectomy [2–6]; a two-incision VATS for anatomical pulmonary resection was performed by different groups [7–12], and a standardized three-port approach was described by different authors [13–17]. Although the potential advantages of a one-incision (uniportal) approach have not been demonstrated to date, it does seem reasonable to consider that the use of only one incision and only one interspace may result in less pain. The objective of this article is to determine if uniportal video-assisted lobectomy is superior to other video-assisted thoracoscopic lobectomy techniques (Duke approach and Copenhagen approach), taking into account the factors, in practice, we consider most relevant.

MATERIALS AND METHODS

This study has been approved by the research ethics committee in Balearic Island Region. The trial was registered in the EudraCT

database (number 2015-005603-81), and reporting was guided by the principles outlined in the CONSORT 2010 statement [18].

We conducted an assessor-blinded, 1:1 parallel-group, randomized controlled trial. Eligible participants were patients scheduled for pulmonary resection at the Department of Thoracic Surgery, Hospital Universitario Son Espases, on the suspicion of a confirmed lung tumour. Inclusion criteria were: T1 or T2 tumours; peripherally located tumours; centrally placed tumours but not adherent to vessels. Excluded cases were those in which the patient did not give his (her) consent to take part in the study (5 cases), and patients with chronic ingestion of analgesics, steroids or opiates: this is due to the possibility of biases in assessing postoperative pain (20 cases).

We used a computer-generated randomization list with alternate blocks of 4–6. Group allocations were placed and kept by an independent person in sequentially numbered sealed opaque envelopes and released to the main researcher individually and in sequential order at the point of randomization. Patients were allocated to either uniportal video-assisted lobectomy (Group A) or other video-assisted thoracoscopic lobectomy techniques (Group B) after the written consent was obtained, 1 working day prior to the surgery. Randomization results were disclosed by the main researcher (Valerio Perna).

All our patients have a preoperative examination with lung function testing, positron emission tomography/computed tomography (PET/CT), bronchoscopy and EBUS/mediastinoscopy for preoperative staging (unless it is a peripherally placed T1 tumour on PET). Patients were randomized in two groups: A (patients treated by uniportal video-assisted lobectomy) and B (patients treated by Duke approach and Copenhagen approach). The interventions were done by four senior staff thoracic surgeons using identical criteria. A 28F pleural drainage tube was placed in all of the patients and it was connected to continuous aspiration for a minimum of 24 h. We established two removal criteria: (i) No evidence of air leak. (ii) Pleural drainage less than 150 ml in the last 24 h. All cases were treated with prophylactic antimicrobials: cefazolin 2 g at the start of anaesthesia. A paravertebral catheter is inserted for a minimum of 24 h: continuous infusion, through an elastomeric pump, of 1.25 mg ml^{-1} levobupivacaine plus 1 μg ml^{-1} fentanil, set at a rate of 5 ml h; when supplementary analgesics were needed (level of pain higher than 7 in the analogue visual scale), up to three doses per day of morphine (5 mg endovenously) were injected. The patient was discharged, barring other complications, 24 h after the removal of the drainage tube. Postoperative follow-up included patient visits and roentgenograms, which were continued after 1 and 3 months.

In the study design, we rely on the only prospective observational study published in the literature applying the following changes: randomization, evaluation of postoperative pain during the first 3 days (to identify possible differences coinciding with discontinuing patient-controlled analgesia and with starting of mobilization) and valuing the type of resection, R0/R1 (a very important factor in assessing postoperative pain) [19].

The primary outcome measures were: (i) median patient reported pain score in the first 24 h, median patient reported pain score on the second postoperative day and median patient reported pain score on the third postoperative day. To evaluate the pain, we used the visual analogue scale: 'no pain' score of 0 and 'pain as bad as it could be' or worst imaginable pain' score of 10 [20, 21]. (ii) The total amount of supplementary analgesic dosage (morphine, milligrams) in the first 24 postoperative hours, on the second postoperative day and on the third postoperative day.

The delay in removing the paravertebral catheter and the chest drain, the duration of the postoperative hospital stay, the postoperative complications and the operative or 30-day mortality were the secondary outcomes considered.

Different clinical parameters (age, clinical stage and comorbidity), preoperative and pathological variables were also recorded.

STATISTICAL ANALYSIS

Sample size was set to reach a statistical power of 80% to detect an expected difference in postoperative pain of at least two points (visual analogue score for pain). χ^2 test was used for the calculation.

Continuous variables were evaluated for normality with the D'Agostino–Pearson test. Normally distributed data were expressed as mean values with 95% confidence intervals. Means were compared with independent samples *t*-test. Non-normal data were expressed as median values with interquartile ranges. Medians were compared with the Mann–Whitney *U*-test. Categorical data were analysed with Fisher's exact test.

The series along with the clinical parameters, preoperative and pathological variables and outcomes were dichotomized into uniportal and other video-assisted thoracoscopic lobectomy groups. Statistical significance was accepted when $P < 0.05$.

The statistical workout was performed using SPSS Version 19.0 (SPSS, Chicago, IL, USA).

Surgical techniques

Uniportal video-assisted lobectomy: the incision, about 4–5 cm long, is performed at the fifth intercostal space. We do not use rib retractors. The camera must be at an 30° angle to provide a panoramic view. When there is no angle for stapler insertion (Covidien endo-GIA stapler with tri-staple cartridges) or it is difficult to achieve from the incision, as with the lingular vein or the middle lobe vein, we use vascular clips (Hem-o-Lok Ligation System, ML size). The camera is operated by a team member standing at the patient's anterior side, the same side of the surgeon. Camera placement for the lobectomy and lymph node dissection is usually at the posterior part of the incision, working with the instruments below.

Hilar dissection is always carried out in the same sequence: artery, vein, bronchus. For upper lobectomies, we use the fissureless technique. In the case of lower lobectomies with no artery visible in the fissure, the procedure must be performed from bottom to top, with fissure stapling as the final step. When the lobectomy is completed, the lobe is removed in a protective bag and a systematic lymph node dissection is conducted. Once operation is completed, we insert a single chest tube in the posterior part of the incision.

Duke approach: a 4 cm access incision is made anteriorly, and the fifth intercostal space is opened, ∼1 cm more anterior and posterior than the extent of the skin incision. Adjacent and posterior to the incision, a 5 mm camera port incision is made. A 5 mm 30° thoracoscope is placed within a trocar. The camera is operated by a team member standing at the back side of the patient, and the surgeon stands at the patient's anterior side. Hilar dissection is carried out through the anterior incision, as with the standard two-incision VATS resection. Dissection of the pulmonary vessels and bronchi is performed beginning anteriorly and continuing posteriorly. Endoscopic linear staplers are used for individual vessel

and bronchial ligation (Covidien endo-GIA stapler with tri-staple cartridges). Once the lobe is completely resected, it is placed in a specimen bag for retrieval to avoid implantation of tumour cells into the incision. We also perform systematic mediastinal lymph node dissection. A single chest tube for drainage is inserted in the camera incision.

Copenhagen approach: a 5 cm anterior utility incision is made without any tissue retractor or rib spreading. The wound is protected by a plastic soft tissue retractor kept in place by a ring in the chest cavity and one outside the skin (SurgiSleeve, COVIDIEN, USA). This incision is later used for specimen retrieval, and is positioned between the breast and the lower angle of the scapula in the fourth intercostal space just anterior to the latissimus dorsi muscle. The cavity is evaluated with the camera (10 mm, 30° angled video-thoracoscope) through this incision looking for unexpected pathology, adhesions and the level of the diaphragm. A low anterior 1 cm camera port is positioned at the level of the top of the diaphragm and anterior to the level of the helium and the phrenic nerve. The camera is operated by a team member standing at the patient's anterior side, the same side of surgeon. The final 1.5 cm incision is positioned at the same level but more posterior in a straight line down from the scapula and anterior to the

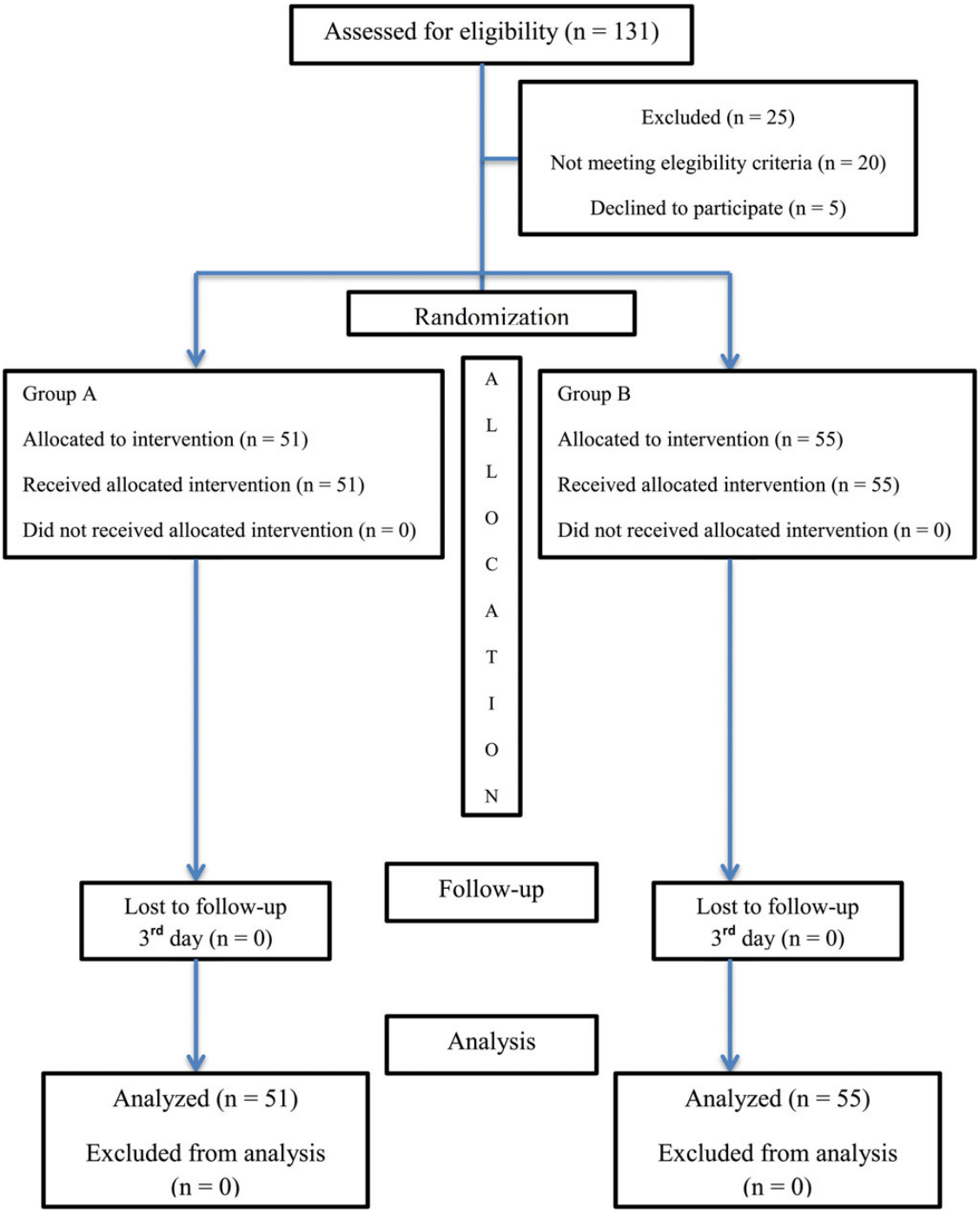

Figure 1: Study flow chart.

latissimus dorsi muscle. This results in a triangle with two ~10 cm limbs and the camera is positioned at the apex, with a working channel on each side. The vessels, the fissure and the bronchus are divided sequentially, with appropriate endostaplers (Covidien endo-GIA stapler with tri-staple cartridges). Any specimen is removed with an endobag. We also perform systematic mediastinal lymph node dissection. At the end, one intercostal drain is placed in through the camera incision.

RESULTS

A flow chart of the trials' progress is depicted in Fig. 1.

One hundred and six patients underwent videothoracoscopy lobectomy at our institution between 2013 and 2015. Fifty-one patients were randomized to receive treatment by uniportal video-assisted lobectomy (Group A) and 55 patients by other video-assisted thoracoscopic lobectomy techniques (26 by Duke approach and 29 by Copenhagen approach). The clinical parameters of the two groups are displayed in Table 1.The mean surgical time, the side of resection, the rate of R0 resection, the clinical and pathological stage, the histology and the mean of lymph node resections are described in Table 2. The clinical stage III is determined by N2 disease in all cases. The pathological stage III is determined by the involvement of one N2 station in all cases.

Regarding postoperative pain, there were no significant differences between the two groups in the first 24 postoperative hours ($P = 0.58$), on the second postoperative day ($P = 0.64$) and on the third postoperative day ($P = 0.85$).

The supplementary doses of analgesic required (morphine, milligrams) did not show statistically significant differences between the two groups during the first 24 h, $P = 0.72$, on the second postoperative day, $P = 0.81$ and on the third postoperative day, $P = 0.64$ (Table 3).

There was no difference in timing to remove the paravertebral catheter ($P = 0.82$) and the chest drain ($P = 0.65$) and in the duration of the postoperative hospital stay ($P = 0.62$). There was no difference in postoperative complications (one case of reoperation for bleeding in the Group B, $P = 0.24$). There was no operative or 30-day mortality in either group (Table 4).

Table 1: Patient demographics with interquartile and confidence interval: Group A and Group B

	Group A	Group B
Patients, *n*	51	55
Gender (M:F)	35:16 (68.6% male)	35:20 (63.6% male)
Median age (years)	69 (65, 76)	72 (68, 79)
ASA grade		
1	12 (23.5%)	14 (25.4%)
2	37 (72.5%)	40 (72.7%)
3	2 (3.9%)	1 (1.8%)
4	0 (0%)	0 (0%)

ASA: American Society of Anesthesiologist.

Table 2: Preoperative and pathological variables

Variables	Group A	Group B
Patients, *n*	51	55
Mean surgical time (min)	152.1 ± 44	145.1 ± 52
Side		
RUL:RML:RLL	15:4:10	15:6:11
LUL:LLL	13:9	12:11
Rate of R0 resection	100%	100%
Clinical stage		
I	15 (29.4%)	14 (25.4%)
II	22 (43.1%)	27 (49.1%)
III	14 (27.4%)	14 (25.4%)
Pathological stage		
I	14 (27.4%)	15 (27.3%)
II	21 (41.2%)	25 (45.4%)
III	16 (31.3%)	15 (27.3%)
Histology		
ADC	35 (68.6%)	38 (69.1%)
SCC	16 (31.4%)	17 (30.9%)
Mean LN resections	14.6 ± 6.8	15.1 ± 6.3

RUL: right upper lobe; RML: right middle lobe; RLL: right lower lobe; LUL: left upper lobe; LLL: left lower lobe; ADC: adenocarcinoma; SCC: squamous cell carcinoma; LN: lymph node.

COMMENT

This study was designed to obtain conclusions about benefits of uniportal approach over other techniques (Duke approach and Copenhagen approach).

Table 3: Primary outcomes: Group A and Group B

	Group A	Group B	*P*-value
Patients, *n*	51	55	
Median VAS in the first 24 h	3	3	0.58
Median VAS on the second day	2	2	0.64
Median VAS on the third day	1	1	0.85
Median morphine use in the first 24 h (mg)	14	11	0.72
Median morphine use on the second day (mg)	8	7	0.81
Median morphine use on the third day (mg)	2	2	0.64

VAS: visual analogue pain score.

Table 4: Secondary outcomes with interquartile and confidence interval: Group A and Group B

	Group A	Group B	*P*-value
Patients, *n*	51	55	
Median duration of PVC	1 (1, 1)	1 (1, 2)	0.82
Median duration of chest drain (days)	2 (2, 3)	2 (1, 4)	0.65
Median in-hospital stay (days)	3 (2, 5)	3 (2, 5)	0.62
Reoperation	0	1	0.24
Operative or 30-day mortality	0	0	1

PVC: paravertebral catheter.

The chosen topic may be considered to be of minor importance, but the truth is that in the last 3–4 years, potential benefits of single-port technique over other endoscopic techniques have been discussed in all courses/conferences on thoracic surgery. In this respect, our study undoubtedly analyses a really burning topic in the specialty. The surgical techniques employed were the most accepted by current surgical groups. 'Three-port' and 'two-port' are historically the most frequently employed techniques to realize a VATS lobectomy. The first uniportal VATS lobectomy was described in 2010. One potential advantage of uniportal approach may be a reduction in postoperative pain. There could be several explanations for this: undoubtedly the most important one is that only one intercostal space is involved, and avoiding the use of a trocar could minimize the risk of intercostal nerve injury. For this reason, the primary outpoint we considered in the study was postoperative pain. We rely our study on the only prospective observational study published in the literature [19] to evaluate if a randomized design, taking into account factors such as patient mobilization and complete resection, could show statistically significant differences between the two groups. Up to date, no prospective, randomized study has been published that directly compares the uniportal with other video-assisted thoracoscopic lobectomy approaches. With our series, we have confirmed the results described by McElnay *et al.* eliminating all factors of major bias [19].

Regarding the secondary outcomes, all postoperative variables considered are similar between the two groups, so we may conclude that the techniques used in the two groups are reasonably non-traumatic, with little morbidity for the patient.

The main strength of this study is a randomized and prospective design. The main weakness is the *n*: while it is not tiny, it is also not particularly large. In fact, we have grouped the 'two-port' and 'three-port' procedures in the analysis because of this problem. In conclusion, uniportal video-assisted lobectomy is not related with better postoperative outcomes when compared with two- or three-port approach. Anyway, it is necessary to confirm these results by further randomized prospective trials with a larger number.

Conflict of interest: none declared.

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